# Original articles

## Nutritional status of patients referred for hyperbaric oxygen treatment; a retrospective and descriptive cross-sectional study

Rutger C Lalieu[1,2], Ida Akkerman[3], Peter-Jan AM van Ooij[4,5], Annieke A Boersma-Voogd[4,6], Rob A van Hulst[2,4]

[1] *Hyperbaric Center Rijswijk, Rijswijk, the Netherlands*
[2] *Hyperbaric and Diving Medicine, Anesthesiology, Amsterdam Medical Centre, Amsterdam, the Netherlands*
[3] *Independent researcher, de nieuwe delta, Ede, the Netherlands*
[4] *Antonius Hypercare, Sneek, the Netherlands*
[5] *Diving Medical Center, Royal Netherlands Navy, Den Helder, the Netherlands*
[6] *Independent researcher, Dieetstyle – Annieke Boersma, Sneek, the Netherlands*

***Corresponding author:*** *Dr Rutger C Lalieu, Hyperbaric Center Rijswijk, Treubstraat 5A, 2288 EG Rijswijk, the Netherlands*
*r.lalieu@hgcrijswijk.nl*

**Key words**
Hyperbaric medicine; Hyperbaric research; Irradiation; Nutrition; Obesity; Osteoradionecrosis; Wounds

**Abstract**
(Lalieu RC, Akkerman I, van Ooij PJAM, Boersma-Voogd AA, van Hulst RA. Nutritional status of patients referred for hyperbaric oxygen treatment; a retrospective and descriptive cross-sectional study. Diving and Hyperbaric Medicine. 2021 December 20;51(4):322–327. doi: 10.28920/dhm51.4.322-327. PMID: 34897596.)

**Introduction**: Due to the global rise of obesity, the role of nutrition has gathered more attention. Paradoxically, even overweight persons may be malnourished. This may delay wound healing or recovery of late radiation tissue injury (LRTI). Hyperbaric oxygen treatment (HBOT) is used to improve wound healing or LRTI complaints. The aim of this study was to assess the dietary intake levels of nutrients important for recovery in patients referred for HBOT.

**Methods**: This was a retrospective, cross-sectional study of patients referred for HBOT to a single centre between 2014 and 2019. Patients were offered a consultation with a dietitian as standard care. Information on nutrients was calculated from questionnaires, and compared to recommended daily allowances.

**Results**: One hundred and forty-six patients were included (80 female). Eighteen patients were treated for diabetic ulcers, 25 for non-diabetic ulcers and 103 for LRTI. Most were overweight or obese (64.4%), but did not consume the recommended quantities of calories, protein, or micronutrients. Vitamin C consumption was higher than recommended. Male patients had a higher intake of calories and protein than female patients but not other nutrients. No differences in intake existed between age or body mass index categories.

**Conclusions**: The nutritional status of patients referred for HBOT may be inadequate for healing wounds or LRTI, despite anthropomorphic data indicating a positive energy balance. Daily attendance for HBOT provides a unique opportunity to monitor and correct these deficiencies. Routine screening for malnutrition and supplement deficiencies is recommended for patients referred for HBOT.

### Introduction

The important role of adequate nutrition in health has long been known. Over the last few years it has garnered increased attention due of the global rise in obesity.[1] Paradoxically, the presence of increased body mass index (BMI) does not translate to being well-fed. In fact, overweight people can still suffer from nutrient deficiencies, or malnutrition.[2] The worldwide prevalence of malnutrition is, therefore, high but often unrecognised, and is associated with adverse clinical outcomes and costs.[3]

Wound healing is one example of health that is negatively impacted by malnutrition.[4] Energy demand may be up to 50% higher than usual.[5] Nutritional deficiencies can prolong the inflammatory phase, decrease fibroblast proliferation and alter collagen synthesis, which may lead to a non-healing wound.[6] Elderly persons are especially at risk for this due to underlying comorbidities.[7] When ulcers become chronic, they can cause pain and other physical discomforts,[8] while quality of life is also negatively impacted.[9] They are also an economic burden, influencing health care budgets[10] and causing loss of work.[9] Non-healing ulcers, especially diabetic ulcers, may result in amputation of digits or limbs.[11] After amputation, overall mortality rate is significantly increased.[12] Due to increased life expectancy, the number of chronic wounds and associated costs is expected to rise in the coming years.[13]

Another example is late radiation tissue injury (LRTI). Radiation injury after head and neck cancer can present as osteoradionecrosis of the jaw,[14] which leads to dental pain, reduced oral intake and as a consequence, weight loss and low BMI.[15] Pelvic radiation may cause radiation enteritis and thus malabsorption of nutrients, leading to the same outcome.[16]

In both groups of patients, malnutrition may contribute to failure in wound healing as well as increased risk of postoperative complications, including infections, delayed recovery, and increased mortality.[17]

Hyperbaric oxygen treatment (HBOT) may be used to facilitate healing of both chronic wounds and LRTI.[18] The treatment involves inhalation of 100% oxygen under increased atmospheric pressure, and usually takes place daily for several weeks. The daily patient contact provides a unique opportunity to identify and monitor nutritional status in this at-risk population. Indeed, a recent study found that one-third of a population treated with HBOT were moderately or severely malnourished.[17] The aim of the current study was to assess the dietary intake levels of nutrients important for wound healing and recovery from LRTI in patients referred for HBOT to a single centre over a period of six years.

## Methods

This study was approved by the local Medical Ethical Commission.

This study uses a retrospective and descriptive cross-sectional design to assess the dietary intake levels of nutrients for wound healing and general health. All patients treated in the hyperbaric centre of the Antonius hospital in Sneek, the Netherlands, are offered a consultation with a clinical dietitian (AB) as part of their standard care. All patients treated between 2014 and 2019 were eligible for inclusion in the current study. Patients were solely treated for chronic (diabetic) wounds and LRTI; no acute indications were treated. Patients who had been treated earlier at this centre, and thus already received advise on improving nutrition, were excluded. Additional exclusion criteria were the standard safety exclusion criteria for HBOT. No other exclusion criteria were applied. The data from the dietary consultation was generated as part of regular care and anonymously and retrospectively used in the current study.

The dietitian took a standard recall questionnaire of a single 24-hour midweek food intake period and entered this into a software system (Nevo-Online, version 5.0, 2016). The Dutch Food Composition Database (NEVO) contains data on the composition of foods. NEVO is owned by the Dutch Ministry of Health, Welfare and Sports, and is maintained at the Dutch National Institute for Public Health and the Environment (RIVM). Data generated included a nutrient analysis of the patient-reported diet on a per-day basis. The software programme extracts information on 26 nutrients from the entered data, including calories, proteins, fats and several vitamins and trace elements. Based on age, gender and body composition, a personal recommended daily allowance (RDA) was calculated. For vitamins and minerals, a standard RDA was provided based on European guidelines.[19] The increased nutritional requirements for wound healing were also taken into account when calculating the RDA. When deficiencies were found, supplements were prescribed. Vitamin C was always supplemented, as recommended for complex wound healing.[6] See Appendix 1* for an example calculation.

For this study, information on calories, proteins, iron, zinc and vitamins A, C, D and E was collected. Age and gender were recorded, and height and weight were measured to calculate BMI. BMI was categorised as underweight (< 18.5 $kg \cdot m^{-2}$), normal weight (18.5–24.9), overweight (25–29.9) and obese (> 30). The different treatment indications were categorised as LRTI and diabetic or non-diabetic wounds; LRTI was further split into different body regions (e.g., breast, head and neck, colorectal, etc.).

### STATISTICAL ANALYSIS

Descriptive statistics for continuous variables were reported as medians with interquartile ranges. Discrete variables were reported as numbers and percentages. Comparisons of intake of all nutrients between gender, age (continuous) and BMI categories and different indications were made with one-way ANOVA. Daily intake of all nutrients was compared against the RDA for female and male patients separately. Since the data were not normally distributed after a Shapiro-Wilk test, a Wilcoxon signed-rank test was performed for the comparison. The null hypothesis for each test was that there is no difference between groups and that daily intake does not differ from the recommended intake. A $P$-value < 0.05 was considered statistically significant for all tests. All statistical analyses were performed with SPPS version 26 (IBM, New York, USA).

## Results

During the study period, 146 patients were included, of which 80 were female (54.8%). Eighteen patients were treated for a diabetic ulcer, 25 patients for a non-diabetic ulcer and 103 patients for LRTI. The median age was 66 years (interquartile range [IQR] 53 to 74) and the median BMI was 26.4 $kg \cdot m^{-2}$ (IQR 23.8 to 29.5). Most patients (41.8%) were overweight (Table 1).

**Footnote:** * Appendix 1 is available on DHM Journal's website: https://www.dhmjournal.com/index.php/journals?id=287

**Table 1**
General description of population; data are median (interquartile range) or *n* (%); BMI – body mass index; LRTI – late radiation tissue injury

| Parameter | Total *n* = 146 | Female *n* = 80 | Male *n* = 66 |
|---|---|---|---|
| Age (years) | 66 (53–74) | 59 (51–72) | 70 (61–77) |
| BMI ($kg \cdot m^{-2}$) | 26.4 (23.8–29.5) | 27.1 (23.3–31.8) | 25.9 (24.5–28.7) |
| Underweight (BMI < 18.5) | 3 (2.1) | 2 (2.5) | 1 (1.5) |
| Normal weight (BMI 18.5–24.9) | 49 (33.6) | 26 (32.5) | 23 (34.8) |
| Overweight (BMI 25–29.9) | 61 (41.8) | 30 (37.5) | 31 (47.0) |
| Obese (BMI > 30) | 33 (22.6) | 22 (27.5) | 11 (16.7) |
| Diabetic wound | 18 (12.3) | 8 (10.0) | 10 (15.2) |
| Non-diabetic wound | 25 (17.1) | 10 (12.5) | 15 (22.7) |
| LRTI | 103 (70.5) | 62 (77.5) | 41 (62.1) |
| Breast | 36 (35.0) | 36 (58.1) | – |
| Head and Neck | 10 (9.7) | 3 (4.8) | 7 (17.1) |
| Urologic | 27 (26.2) | 5 (8.1) | 22 (53.7) |
| Gynaecologic | 8 (7.8) | 8 (12.9) | – |
| Colorectal | 10 (9.7) | 4 (6.5) | 6 (14.6) |
| Other | 12 (11.7) | 6 (9.7) | 6 (14.6) |

Median daily intake and RDA of all nutrients are reported in Tables 2 and 3 for females and males respectively. Also included is the number of patients that managed to reach their RDA. Most patients did not consume the amounts of calories, protein, vitamins A and D and zinc that were recommended for them. Conversely, around 70% of patients consumed vitamin C above the recommended level. More female patients achieved their RDA of calories and protein than male patients. For iron, more male patients achieved their RDA than female patients. There was no gender difference in intake of other nutrients. Furthermore, no differences in intake existed between age or BMI categories (findings not shown). Although there were statistically significant differences in vitamin A intake between the breast, head and neck and other LRTI categories, this was not considered clinically relevant. No other differences were found between LRTI subgroups.

## Discussion

These data show that nutrition status is suboptimal in most patients referred for HBOT with wound healing problems or LRTI, despite the fact that more than 60% were overweight or obese based on BMI. This may not immediately impact general health but may prolong already delayed healing of wounds or LRTI. The results confirm those reported previously,[17] in which 30% of patients referred for HBOT were at risk for malnourishment.

Calories and protein are well-known factors that influence healing processes in the human body. The number of calories consumed per day is a measure of energy, which may be produced from different sources, such as carbohydrates, protein or fats.[6,20] Other than a source of energy, proteins are used for tissue growth, can be broken down to amino acids, and be used for synthesis of different proteins.[4,20] Some of these amino acids are essential, meaning they cannot be synthesised by the body but need to be derived from intake of food. The uptake and utilisation of proteins is partly dependent on certain vitamins and trace elements, such as zinc.[20] Vitamin A is derived from carotenoids in vegetables that enhances the early inflammatory phase and plays a role in the proliferation and re-epithelization phases.[4,20] Vitamin C is a cofactor for collagen synthesis, reduces reactive oxygen species (ROS) and facilitates uptake of iron, among many other roles.[20] Vitamin D plays an important role in the regulation of cell proliferation and differentiation, and in the modulation of immune system responses. There is growing evidence it might protect against cancer, prediabetes and metabolic syndrome.[21] The role of vitamin E is mostly that of antioxidant, reducing ROS and thereby limiting their deleterious effects on cell membranes, and facilitating wound healing.[4,20] Zinc is a cofactor for major enzyme systems, facilitates carbohydrate metabolism and plays a role in uptake of certain vitamins, such as vitamin A.[4,20] Finally, iron is used in heme in red blood cells to facilitate oxygen transport, and iron deficiency may lead to anaemia. It also plays a role in mitochondrial respiration and immune function.[22]

There is ample research on the role of nutrients in wound healing in the human body.[4] While LRTI may lead to non-healing wounds, the underlying mechanism differs from other chronic wounds such as diabetic ulcers. Exposure to ionising radiation produces ROS,[23] causing direct damage to DNA and proteins, which in turn leads to cell death.[24] This

**Table 2**

Female patients; intake and recommended amounts of nutrients, and numbers of patients achieving recommended daily allowance (RDA); † – RDA based on gender, age, and body composition; * RDA for age > 50 years = 10 µg·day$^{-1}$, > 70 years = 20 µg·day$^{-1}$

| Parameter | Calories (kcal·day$^{-1}$) | | Protein (g·day$^{-1}$) | | Vitamin A (µg·day$^{-1}$) | | Vitamin C (mg·day$^{-1}$) | | Vitamin D (µg·day$^{-1}$) | | Vitamin E (mg·day$^{-1}$) | | Zinc (mg·day$^{-1}$) | | Iron (mg·day$^{-1}$) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Intake | RDA† | Intake | RDA† | Intake | RDA | Intake | RDA | Intake | RDA* | Intake | RDA | Intake | RDA | Intake | RDA |
| 25$^{th}$ percentile | 1,350 | 1,978 | 64.0 | 80.0 | 335.0 | 800.0 | 67.5 | 75.0 | 1.7 | 10.0 | 6.0 | 8.7 | 7.9 | 10.0 | 7.1 | 10.8 |
| Median | 1,517 | 2,178 | 71.0 | 86.5 | 456.0 | | 90.0 | | 2.7 | | 8.6 | | 9.0 | | 8.4 | |
| 75$^{th}$ percentile | 1,808 | 2,350 | 80.0 | 95.8 | 558.8 | | 115.5 | | 3.7 | | 11.2 | | 10.0 | | 10.2 | |
| RDA achieved, *n* (%) | 8 (10.0) | | 19 (23.8) | | 10 (12.8) | | 57 (71.3) | | 3 (3.8) | | 43 (53.8) | | 22 (27.5) | | 31 (38.8) | |
| Intake versus RDA | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P = 0.339$ | | $P < 0.01$ | | $P = 0.005$ | |

**Table 3**

Male patients; intake and recommended amounts of nutrients, and numbers of patients achieving recommended daily allowance (RDA); † – RDA based on gender, age, and body composition; * RDA for age > 50 years = 10 µg·day$^{-1}$, > 70 years = 20 µg·day$^{-1}$

| Parameter | Calories (kcal·day$^{-1}$) | | Protein (g·day$^{-1}$) | | Vitamin A (µg·day$^{-1}$) | | Vitamin C (mg·day$^{-1}$) | | Vitamin D (µg·day$^{-1}$) | | Vitamin E (mg·day$^{-1}$) | | Zinc (mg·day$^{-1}$) | | Iron (mg·day$^{-1}$) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Intake | RDA† | Intake | RDA† | Intake | RDA | Intake | RDA | Intake | RDA* | Intake | RDA | Intake | RDA | Intake | RDA |
| 25$^{th}$ percentile | 1,491 | 2,300 | 65.5 | 93.0 | 365.0 | 900.0 | 72.5 | 75.0 | 2.3 | 10.5 | 6.9 | 10.0 | 7.8 | 10.0 | 7.6 | 9.0 |
| Median | 1,757 | 2,616 | 75.5 | 98.0 | 500.0 | | 99.0 | | 3.1 | | 9.6 | | 9.0 | | 9.1 | |
| 75$^{th}$ percentile | 1,992 | 2,814 | 90.0 | 105.3 | 674.0 | | 123.8 | | 4.0 | | 10.9 | | 10.8 | | 10.6 | |
| RDA achieved, *n* (%) | 4 (6.1) | | 11 (16.7) | | 9 (13.6) | | 47 (71.2) | | 2 (3.0) | | 30 (45.5) | | 25 (37.9) | | 35 (53.0) | |
| Intake versus RDA | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P < 0.01$ | | $P = 0.129$ | | $P = 0.042$ | | $P = 0.776$ | |

also leads to loss of vascular tissue, causing hypoxia, and an overproduction of proinflammatory markers in the radiated tissue.[25] This hypoxic and proinflammatory state persists even after radiotherapy has ended,[26] and this continued inflammation is one of the most important factors causing LRTI.[27] HBOT may be used to improve tissue oxygenation and decrease circulating levels of proinflammatory cytokines.[28] However, it also leads to increased production of ROS. Antioxidants counter the production of ROS, and since exposure to hyperoxia during HBOT is usually limited, normal levels of antioxidants are usually adequate to counter the extra production caused by HBOT.[28] In the human body, certain enzymes act as antioxidants, but there are also non-enzymatic antioxidants, such as vitamins C and E, which can be acquired from food.[28] Eating food rich in these vitamins is recommended to maintain an adequate supply.[29] Since most people are aware of the beneficial properties of vitamin C, this is probably the reason why this is consumed more than average. While not an antioxidant itself, zinc can help maintain enzymatic antioxidants.[29]

## STRENGTHS AND LIMITATIONS

The above list of nutrients is not exhaustive when it comes to wound healing or other regenerative processes. The vitamin B complex, magnesium and lipids are examples of other nutrients that are necessary in wound healing.[4,20] Therefore, this study gives an incomplete picture. However, it is argued that since most of the nutrients reported are already deficient in this population, this will not be different for other nutrients. Another limitation of this study is the method of data gathering. A single 24-hour period was used to measure average intake, and intake on other days and weekends may very well differ from this measurement. However, this short time-period was deliberately chosen, as keeping a week-long food diary was considered too impactful next to HBOT. Furthermore, questionnaires are inherently biased since patients may forget or choose to omit certain foods on it. For future studies specifically looking at nutrients, a food diary spanning multiple days may improve accuracy. Although biomarkers in urine or blood samples might also provide more information regarding a person's nutritional status, these biomarkers are not specific enough to detect malnutrition.[30] However, they can be used as an early signal of certain deficiencies.[30] A last limitation is the population itself, which is mostly composed of patients from a northern province of the Netherlands which is not as densely populated or urbanised as other parts. Although there are no specific data on this topic, dietary habits (and thereby nutrition) may differ from persons living in other parts of the Netherlands.

Aside from these limitations, the strength of the current study is the inclusion of a relatively large group of patients with different morbidities. This is likely a representative sample of the population that is usually referred for HBOT in the Netherlands. Furthermore, data on intake and personal RDA of a large number of nutrients are included, instead of only dietary habits or certain food groups. This provides an opportunity for direct supplementation and a more targeted approach.

## Conclusions

The current study adds to the literature by highlighting that energy, protein and micronutrient intake may be suboptimal in patients attending HBOT. This may be because they cannot meet the increased metabolic demand presented by their affliction. The daily attendance for HBOT provides a unique opportunity to monitor and correct these deficiencies. However, a robust, prospective study with a large population is warranted to further examine the specific deficiencies that may be present in this population. These data should be further contextualised with treatment results and quality of life parameters. In the meantime, it is recommended to routinely screen patients referred for HBOT for nutritional intake and to supplement deficiencies when necessary.

## References


1 Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism. 2019;92:6–10. doi: 10.1016/j.metabol.2018.09.005. PMID: 30253139.

2 Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the double burden of malnutrition and the changing nutrition reality. Lancet. 2020;395(10217):65–74. doi: 10.1016/S0140-6736(19)32497-3. PMID: 31852602. PMCID: PMC7179702.

3 Watterson C, Fraser A, Banks M, Isenring E, Miller M, Silvester C. Evidence based practice guidelines for the nutritional management of malnutrition in adult patients across the continuum of care. Nutr Diet. 2009;66:S1–S34. doi: 10.1111/j.1747-0080.2009.01383.x.

4 Bishop A, Witts S, Martin T. The role of nutrition in successful wound healing. J Community Nurs. 2018;32(4):44–50. [cited 2021 Oct 10]. Available from: https://www.ddrc.org/app/uploads/2018-Bishop-A-Witts-S-Martin-The-role-of-nutrition-in-successful-wound-healing-JCN.pdf.

5 Demling RH. Nutrition, anabolism, and the wound healing process: an overview. Eplasty. 2009;9:e9. PMID: 19274069. PMCID: PMC2642618.

6 Stechmiller JK. Understanding the role of nutrition and wound healing. Nutr Clin Pract. 2010;25:61–8. doi: 10.1177/0884533609358997. PMID: 20130158.

7 Harris CL, Fraser C. Malnutrition in the institutionalized elderly: the effects on wound healing. Ostomy Wound Manage. 2004;50(10):54–63. PMID: 15509882.

8 Snelgrove H, Baileff A. A review of interventions to reduce pain in chronic wounds. Br J Community Nurs. 2019;24(Supp 12):S12–S17. doi: 10.12968/bjcn.2019.24.Sup12.S12. PMID: 31804887.

9 Kapp S, Miller C, Santamaria N. The quality of life of people who have chronic wounds and who self-treat. J Clin Nurs. 2018;27:182–92. doi: 10.1111/jocn.13870. PMID: 28493644.

10 Sen CK. Human wounds and its burden: an updated compendium of estimates. Adv Wound Care (New Rochelle). 2019;8(2):39–48. doi: 10.1089/wound.2019.0946. PMID: 30809421. PMCID: PMC6389759.

11 Järbrink K, Ni G, Sönnergren H, Schmidtchen A, Pang C,

Bajpai R, et al. The humanistic and economic burden of chronic wounds: a protocol for a systematic review. Syst Rev. 2017;6(1):15. doi: 10.1186/s13643-016-0400-8. PMID: 28118847. PMCID: PMC5259833.

12 Cascini S, Agabiti N, Davoli M, Uccioli L, Meloni M, Giurato L, et al. Survival and factors predicting mortality after major and minor lower-extremity amputations among patients with diabetes: a population-based study using health information systems. BMJ Open Diabetes Res Care. 2020;8(1):e001355. doi: 10.1136/bmjdrc-2020-001355. PMID: 32690575. PMCID: PMC7371030.

13 Sen CK, Gordillo GM, Roy S, Kirsner R, Lambert L, Hunt TK, et al. Human skin wounds: a major and snowballing threat to public health and the economy. Wound Repair Regen. 2009;17:763–71. doi: 10.1111/j.1524-475X.2009.00543.x. PMID: 19903300. PMCID: PMC2810192.

14 Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. Int Dent J. 2018;68:22–30. doi: 10.1111/idj.12318. PMID: 28649774.

15 Citak E, Tulek Z, Uzel O. Nutritional status in patients with head and neck cancer undergoing radiotherapy: a longitudinal study. Support Care Cancer. 2019;27:239–47. doi: 10.1007/s00520-018-4319-6. PMID: 29938330.

16 Loge L, Florescu C, Alves A, Menahem B. Radiation enteritis: diagnostic and therapeutic issues. J Visc Surg. 2020;157:475–85. doi: 10.1016/j.jviscsurg.2020.08.012. PMID: 32883650.

17 See HG, Tan YR, Au-Yeung KL, Bennett MH. Assessment of hyperbaric patients at risk of malnutrition using the Malnutrition Screening Tool – a pilot study. Diving Hyperb Med. 2018;48:229–34. doi: 10.28920/dhm48.4.229-234. PMID: 30517955. PMCID: PMC6355311.

18 Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. Diving Hyperb Med. 2017;47:24–32. doi: 10.28920/dhm47.1.24-32. PMID: 28357821. PMCID: PMC6147240.

19 Health Council of the Netherlands. [cited 2021 Oct 10]. Available from: https://www.gezondheidsraad.nl/documenten/adviezen/2018/09/18/gezondheidsraad-herziet-voedingsnormen-voor-volwassenen.

20 Brown KL, Phillips TJ. Nutrition and wound healing. Clin Dermatol. 2010;28:432–9. doi: 10.1016/j.clindermatol.2010.03.028. PMID: 20620761.

21 Geissler C, Powers H. Human nutrition. 12th ed. Churchill Livingstone; 2010.

22 Wlaschek M, Singh K, Sindrilaru A, Crisan D, Scharffetter-Kochanek K. Iron and iron-dependent reactive oxygen species in the regulation of macrophages and fibroblasts in non-healing chronic wounds. Free Radic Biol Med. 2019;133:262–75. doi: 10.1016/j.freeradbiomed.2018.09.036. PMID: 30261274.

23 Borek C. Antioxidants and radiation therapy. J Nutr. 2004;134:3207S–9S. doi: 10.1093/jn/134.11.3207S. PMID: 15514309.

24 Feldmeier JJ. Hyperbaric oxygen therapy and delayed radiation injuries (soft tissue and bony necrosis): 2012 update. Undersea Hyperb Med. 2012;39:1121–39. PMID: 23342770.

25 Denham JW, Hauer-Jensen M. The radiotherapeutic injury - a complex 'wound'. Radiother Oncol. 2002;63:129–45. doi: 10.1016/s0167-8140(02)00060-9. PMID: 12063002.

26 Devalia HL, Mansfield L. Radiotherapy and wound healing. Int Wound J. 2008;5:40–4. doi: 10.1111/j.1742-481X.2007.00351.x. PMID: 18081782. PMCID: PMC7951499.

27 Westbury CB, Yarnold JR. Radiation fibrosis-current clinical and therapeutic perspectives. Clin Oncol (R Coll Radiol). 2012;24:657–72. doi: 10.1016/j.clon.2012.04.001. PMID: 22608361.

28 Thom SR. Oxidative stress is fundamental to hyperbaric oxygen therapy. J Appl Physiol (1985). 2009;106:988–95. doi: 10.1152/japplphysiol.91004.2008. PMID: 18845776. PMCID: PMC2660252.

29 Deb SK, Swinton PA, Dolan E. Nutritional considerations during prolonged exposure to a confined, hyperbaric, hyperoxic environment: recommendations for saturation divers. Extrem Physiol Med. 2016;5:1. doi: 10.1186/s13728-015-0042-9. PMID: 26744625. PMCID: PMC4704397.

30 Keller U. Nutritional laboratory markers in malnutrition. J Clin Med. 2019;8:775. doi: 10.3390/jcm8060775. PMID: 31159248. PMCID: PMC6616535.

**Conflicts of interest and funding:** nil

**Submitted:** 19 May 2021
**Accepted after revision:** 11 September 2021