

The effect of hyperbaric oxygen therapy on pain and quality of life in bone marrow edema

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Abstract

Aim: This study aimed to investigate the effects of ten sessions of Hyperbaric Oxygen Therapy (HBOT) on pain and quality of life in patients with bone marrow edema (BME) who had no specific etiological diagnosis and had previously tried immobilization and analgesic-anti-inflammatory drugs without success.

Methods: This retrospective study involved patients aged 18-65 diagnosed with BME via MRI. Participants underwent ten HBOT sessions in a multi-place pressure chamber at 2.4 ATA for 120 minutes per session. Exclusion criteria included avascular necrosis, active malignancy, advanced osteoarthritis, inflammatory disease, claustrophobia, epilepsy, pregnancy, and lack of consent. The study utilized the SF-12 Quality of Life Scale and Visual Analog Scale (VAS) for pain to measure outcomes before and after HBOT, and data were analyzed using SPSS 25 with appropriate statistical tests.

Results: The study included 64 patients (51.6% female, median age 44). HBOT significantly improved the overall quality of life (mean SF-12 score: before 4366 ± 2006, after 4889 ± 2053, $p=0.034$) and showed notable reductions in pain (mean VAS score: before 7,4 ± 1,2 after 3,8 ± 1,3, $p<0.001$). The male and overweight patients showed more significant benefits.

Conclusion: HBOT is a promising treatment for BME-related pain and quality of life improvement, especially in cases unresponsive to standard therapies. Clinical improvement may begin after just ten sessions of HBOT. The findings suggest that male and overweight patients may benefit more from HBOT, highlighting the need for further research to explore the underlying mechanisms and optimize treatment protocols.

Keywords: Bone marrow, hyperbaric oxygen therapy, pain, quality of life

Introduction

Bone marrow edema (BME) is observed on magnetic resonance imaging (MRI) scans where a substance replaces normal fatty tissue in the bone marrow with a high water content. BME can either be symptomatic or asymptomatic (1). This edema can occur spontaneously or for various reasons and, if associated with pain, can significantly affect the individual's overall health and well-being.

The recovery from BME depends on various factors, including the underlying cause, the patient's overall health, and the type of treatment received. Although BME is most commonly seen in the lower extremities, it is also seen in the pelvis, sacrum, vertebrae, wrist, carpal bones, knees, and bones in the foot (2). The causes of BME may include traumatic, inflammatory/rheumatologic, mechanical/degenerative, neoplastic, ischemic/neurogenic, and metabolic factors. Depending on the etiology of the patient, treatments such as analgesics, anti-inflammatory drugs, immunomodulators, biological therapies, antineoplastics, antibiotics, vitamin D, calcium, bisphosphonates, surgical interventions, physical therapy, and immobilization may be utilized (1).

The treatment aims to alleviate BME symptoms and enhance the patient's quality of life by reducing pain and functional limitations. One potential treatment for BME that has gained attention in recent years is hyperbaric oxygen therapy (HBOT). HBOT is a medical intervention that involves administering pure oxygen to the patient in a pressurized environment, typically in a specialized chamber. This method of treatment is used for a variety of medical conditions ranging from wound healing to decompression sickness and carbon monoxide poisoning. HBOT increases the amount of oxygen dissolved in the patient's blood. The increased partial pressure of oxygen can then be distributed throughout the body. This increased oxygen delivery can help heal hypoxic tissues, directly reduce edema in the bone marrow by vasoconstriction, and indirectly contribute to the improvement of bone marrow edema by promoting angiogenesis, improving venous drainage, improving microcirculation, activating antioxidant mechanisms, and accelerating bone regeneration (3).

This study aimed to investigate the effects of ten sessions of HBOT on pain and quality of life in patients with BME who had not been diagnosed with a specific etiological cause and who had previously tried immobilization and analgesic-anti-inflammatory drugs.

Materials and Methods

This retrospective study received approval from Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee with the date of 25.06.2024 and the number of 125.

It included patients between 18 and 65 years admitted to the Department of Hyperbaric Medicine outpatient unit of Kayseri City Hospital between January and June 2024. The sample size was calculated using the program G*Power version 3.1.9.7 (2020) (University of Düsseldorf, Germany) (for Windows 10), with 80% (beta) power and a type 1 error rate of 0.05 (alpha), with reference to similar studies in the literature, as 57.

These patients were diagnosed with BME in any joint or bone through MRI by a radiologist with over ten years of experience in this field. The patients had no known specific cause for their BME (idiopathic BME). The affected joints or bones of the patients had been previously immobilized, and the patients had received analgesic/anti-inflammatory treatment. Despite these treatments, they still had persistent pain. Therefore, they were considered suitable patients for HBOT. Patients with avascular necrosis on MRI images, active malignancy, advanced osteoarthritis, rheumatologic or inflammatory disease, claustrophobia, epilepsy, pregnancy and patients were not capable of volunteering to participate in the study were excluded from the study. Informed consent was obtained from all patients or their relatives who participated in the study.

The study patients received only HBOT, not any additional therapy. In order to provide standardization, each patient received ten sessions of HBOT in a multi-place pressure chamber at a pressure of 2.4 ATA. Each session lasted 120 minutes with 5-minute air breaks every 25 minutes. The session was held once a day, every weekday. In routine practice, when HBOT is planned for BME patients, the SF-12 Quality of Life Scale and Visual Pain Scale forms are filled out face-to-face with patients both before the first HBOT session and after the last HBOT session (the tenth session). We retrospectively scanned these forms and obtained the data. Demographic data of the patients was also recorded.

Our study used the "SF-12 Quality of Life Scale" to assess all patients' quality of life and physical and mental well-being. This scale is a shortened version of the SF-36 Quality of Life Scale, developed to measure the quality of life. The scale was developed by Gandek (4) in 1998, and the Turkish validity and reliability were assessed in 2022 (5). The scale includes 12 items and eight sub-dimensions, grouped into two main dimensions: The Physical Component Summary (PCS) and the Mental Component Summary (MCS). The PCS comprises four dimensions: physical functioning (2 items), physical role (2 items), general health (1 item), and body pain (1 item). The MCS also comprises four dimensions: social functioning (1 item), emotional role (2 items), mental health (2 items), and energy (1 item). The scale calculates a total score using a point range of 0 to 100. A decrease in scores indicates a decrease in quality of life, while an increase in scores indicates an increase in quality of life. The scale uses a weighted score calculation, and the official SF-36 website was used for this calculation (6).

The Visual Analog Scale (VAS) measured the patient's pain. Participants were asked to score their perception of pain on a 10-cm scale. The scale ranged

from 0 (no pain) to 10 (the most pain) (7). The following cut-off points were used on the scale: mild pain, 0-3

points; moderate pain, 4-7 points; and severe pain, 8-10 points (8). Study flow diagram is shown in Figure 1.

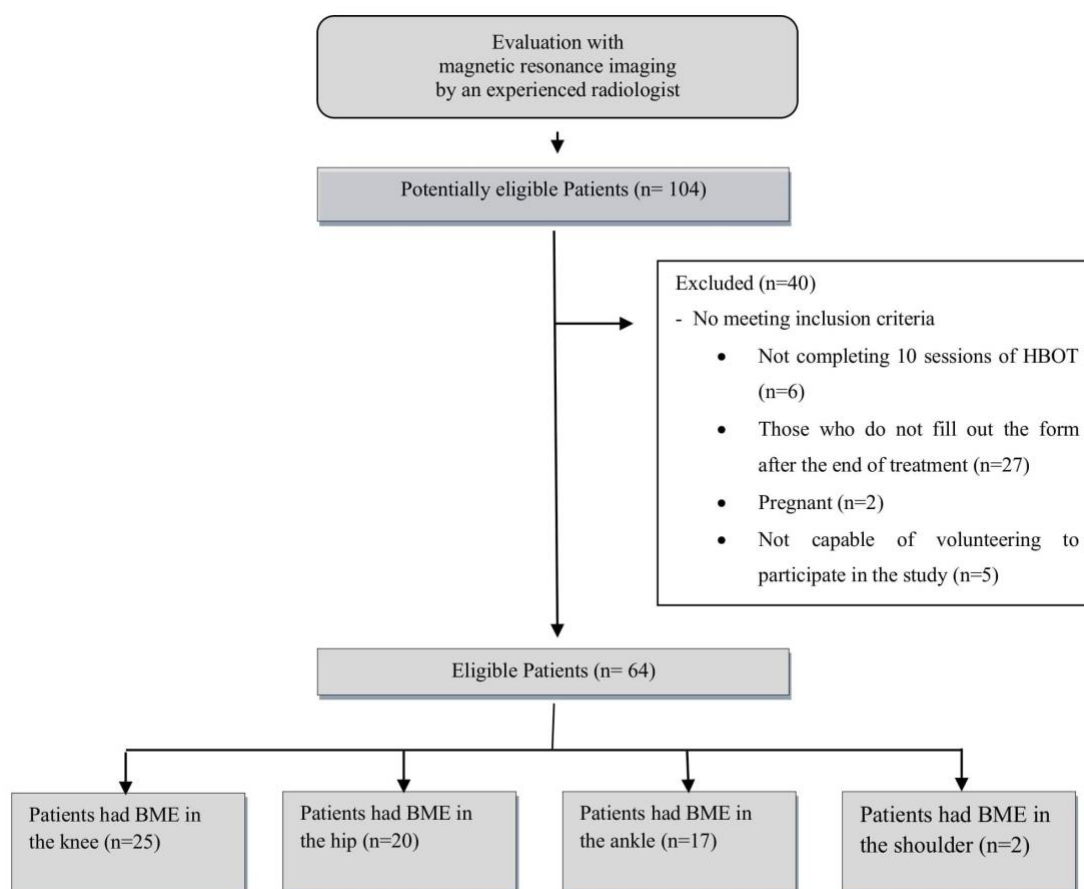


Figure 1. Study flow diagram

Statistical Analysis

Analyses were performed by using SPSS software (IBM SPSS Statistics version 25.0, IBM Inc., Armonk, NY, USA).

The normal distribution of the data was assessed using the Kolmogorov-Smirnov test. Demographic data were presented as mean $\pm$ SD or median (min-max) based on the normality test result. The SF 12 Quality of Life Scale was analyzed in 3 sub-scales: the overall mean of all questions, the mean of the sum of the PCS scores, and the mean of the sum of the MCS scores before treatment and after ten sessions of HBOT using Paired samples t-test. We used several statistical tests to analyze the SF 12 Quality of Life Scale and its subheadings based on demographic data. These included the Mann-Whitney U, Kruskal-Wallis, Independent Sample T, and ANOVA tests. We also used the McNemar-Browker test to compare the changes in response to the pain severity scale questions before and after treatment.

Additionally, we performed Pearson's correlation and Spearman's rho correlation tests to examine the pairwise correlation between the SF 12 Quality of Life

Scale and its subscales. The evaluation of pain scale change was done using a linear regression model. We considered $p < 0.05$ statistically significant at a 95% confidence level

Results

Sixty-four patients who met the inclusion criteria and had complete data available were included in the study. Of these patients, 25 had BME in the knee, 20 in the hip, 17 in the ankle, and 2 in the shoulder (Figure 1). The participants had a median age of 44 years (18-65), a mean height of 167,13 cm $\pm$ 7,42 cm, and a mean weight of 77,94 kg $\pm$ 10,93 kg. The gender distribution was balanced, with 51,6% females and 48,4% males (Table 1).

The data obtained in our study included the overall mean of SF-12 Quality of Life Scale scores and summaries of physical and mental components both before and after treatment. The results indicate that HBOT significantly improved overall quality of life (Table 2).

Table 1. Demographic data

Variable	Mean $\pm$ SD	Median (Min-Max)
Age		44 (18-65)
Height	167.13 $\pm$ 7.42	
Weight	77.94 $\pm$ 10.93	
<u>Variable</u>	<u>N</u>	<u>%</u>
Gender		
Female	33	51.6
Male	31	48.4
Marital Status		
Married	51	79.7
Single	7	10.9
Divorced	6	9.4
Education Status		
Primary Education	12	18.8
Secondary Education		
High School	10	15.6
University		
Master's Degree	23	35.9
	13	20.3
Illiterate	2	3.1
	4	6.3
With whom one lives in the family		
Lives Alone	3	4.7
One lives with wife/husband and children	43	67.2
Lives with wife/husband		
Lives with own's family	8	12.5
	9	14.1
Lives with one's children	1	1.6
Alcohol use		
Yes	3	4.7
No	61	95.3
Smoking Habit		
Yes	15	23.4
No	49	76.6

When the findings analyzing the SF-12 Quality of Life Scale score differences according to demographic data were examined, the median value of the overall total score difference of all questions was found to be 15.00 (min: -440, max: +855). Generally, we observed that

demographic factors, except gender, did not have a statistically significant impact on the effectiveness of HBOT. However, it was noted that male patients showed a more favorable response to the HBOT (Table 3).

Table 2. Mean overall and two dimension averages of SF 12 Quality of Life Scale

Variable	Before Treatment	After Treatment	p
	Mean $\pm$ SD	Mean $\pm$ SD	
Overall Average	43.66 $\pm$ 20.06	48.89 $\pm$ 20.53	0.034
Physical component summary sum of scores (Questions 1-2-3-4-5-8)	34.00 $\pm$ 22.71	39.95 $\pm$ 24.48	0.098
Mental component summary sum of scores (Questions 6-7-9-10-11-12)	53.55 $\pm$ 23.76	57.50 $\pm$ 23.20	0.103

Pair test, SD: Standard Deviation

Table 3. Total score difference for all questions according to demographic data

Variable	Sub Variable	N (%)	Median (Min; Max)	p
Gender	Male	31 (48.4)	70 (- 420; + 855)	0.037*
	Female	33 (51.6)	-45 (- 440; + 520)	
Marital Status	Married	51 (79.7)	5 (- 440; + 650)	0.329*
	Single	13 (20.3)	65 (- 210; + 855)	
Age	< 40 years	16 (25.0)	75 (- 290; + 650)	0.402#
	41-60 age	43 (67.2)	5 (- 440; + 855)	
	>61 years	5 (7.8)	-25 (- 420; + 520)	
BMI ^a	Normal (<24.99)	15 (23.4)	5 (-105;+315)	0.051#
	Overweight (25.00-29.99)	31 (48.4)	80 (-420;+855)	
	Obese (>30.00)	18 (28.1)	-52.5 (-440;+175)	
Education Level	Illiterate	4 (6.3)	17.50 (-440;470)	0.673#
	Primary and Secondary School	22 (34.4)	2.5 (-330;+520)	
	High School	23 (35.9)	45 (-290;+855)	
	University and Above	15 (23.4)	65 (-420;+455)	
Smoking habit	Yes	15 (23.4)	20 (-420;+855)	0.918*
	No.	49 (76.6)	10 (-440;+650)	

*Mann-Whitney U test, #Kruskal-Wallis test, aBMI: Body Mass Index

When the findings analyzing the differences in the scores of the physical component items of the SF-12 Quality of Life Scale according to demographic data were examined, the median value of the difference in scores of the physical component items was found to be 25.00 (min: -350, max: +475). In general, other demographic variables did not affect the difference in physical component scores except for body mass index. Overweight patients experienced more favorable changes in the physical component items.

Our SF-12 Quality of Life Scale analysis found that the average difference in scores for the mental component items was 23.75 $\pm$ 114.80. Our study revealed significant differences in MCS between genders and BMI groups. Men experienced more positive changes in MCS

than women (p=0.040). Additionally, we observed that overweight patients experienced more favorable changes in mental component items compared to obese patients (p=0.029). Other demographic variables such as marital status, age, education level, occupation, and smoking showed no significant effect on the mental component items.

Our study observed a significant decrease in pain level after the treatment (p<0.001). We used the VAS to evaluate patients' pain levels before and after the treatment.

The following findings outline the changes in pain levels before and after the treatment:

- Of the patients who had experienced moderate pain before treatment, 29.27% (12 patients)

showed an improvement to mild pain after treatment. This indicates that the therapy also positively affected patients with moderate pain.

- The treatment reduced pain intensity in most patients experiencing mild to moderate pain, enabling them to report a better pain level.
- A total of 12 patients, representing 66.67% of the patients who experienced severe pain before treatment decreased to milder pain levels after treatment. This shows that the treatment was effective in severe pain.
- The results of the McNemar-Bowker test show that the treatment had a significant effect on pain intensity, and the pain level decreased significantly after treatment ($p < 0.001$) (Table 4).

In addition, a negative correlation was found between the overall total quality of life score and the pain scale ($r = -0.314$, $p = 0.011$). This suggests that pain levels decrease as the overall quality of life increases. Although a weak and negative correlation existed between MSC and pain scale ($r = -0.203$, $p = 0.108$), this relationship was not statistically significant. There was also a weak and negative correlation between PSC and

pain scale ($r = -0.214$, $p = 0.089$), but this relationship was not statistically significant (Table 5).

The regression analysis results showed the impact of the overall difference in quality of life on the change in pain scale. Two different regression models were created, and the results are presented in Table 6. The overall significance of the regression model was assessed with the F test, and the model was found to be significant ($F = 7.656$, $p < 0.007$). This indicates a significant relationship between the dependent variable, pain scale change, and the independent variable, quality of life total difference (Table 6).

The results of the t-test indicated a statistically significant increase in the pain scale change with an increase in the overall total score difference of the participants ($t = 2.767$; $p < 0.007$). The positive effect of the overall total score difference on pain change is confirmed by the standard error ($B = 121.204$, Std. Error = 43.805) and the standardized coefficient ($B = 0.332$). When evaluating the model's explanatory power (goodness of fit), the correlation coefficient ($R = 0.332$) indicates the strength of the relationship between the independent and dependent variables. The R^2 value of 0.110 suggests that the independent variable accounts for 11% of the total variance in the dependent variable. These findings confirm that changes in pain levels significantly and positively impact the overall difference in quality of life (Table 6).

Table 4. Pain severity scale

		After Treatment			
		Light	Medium	Severe	Total
		(1, 2, 3)	(4, 5, 6, 7)	(8, 9, 10)	
Before Treatment	Mild (1,2,3)	4	1	0	5
	Moderate (4,5,6,7)	12	28	1	41
	Severe (8,9,10)	2	10	6	18
	Total	18	39	7	64

$p < 0.001$ (McNemar-Bowker test).

Table 5. Correlation between sub-categories of SF 12 Quality of Life Scale

Variables	Correlation coefficient	<i>p</i>
Grand Total - Physical IC	0.849*	<0.001
Grand Total - Mental IC	0.779*	<0.001
Physical IC - Mental IC	0.376*	0.002
Grand Total - Pain Scale	-0.314 [#]	0.011
Mental IC - Pain Scale	-0.203 [#]	0.108
Physical IC - Pain Scale	-0.214 [#]	0.089

*Pearson , [#] Spearman's rho

Table 6. Regression analysis results

Dependent Variable	Independent Variable	B	Std. Error	B	t	p
General Total	Fixed	7.948	32.854		0.242	0.810
	Pain Change	121.204	43.805	0.332	2.767	0.007
Difference		R= 0.332	R ² = 0.110	F= 7.656	P: 0.007	

B: Unstandardized Coefficient, Std. Error: Standard Error, B: Standardized Coefficient, t: t-value

Discussion

In our study, we observed important results in pain management and quality of life after ten sessions of HBOT in patients with BME who had not been diagnosed with a specific etiological cause. BME is categorized into various types of joint disease and can be grouped as reactive, ischemic, and mechanical. Reactive BME results from an inflammatory response to environmental factors such as arthritis and tumors, while ischemic BME is associated with bone necrosis. Mechanical BME occurs as a result of direct trauma or overload. Treatment options differ depending on the underlying cause and may involve directly addressing the root cause of BME. In some cases, when the cause of BME cannot be attributed to a specific clinical condition, it may be termed "idiopathic BME" (9). Rest, pain control, bisphosphonates, vitamin D and calcium supplementation, prostacyclins, iloprost, denosumab, physiotherapy, and surgical methods are commonly used to treat idiopathic BME, and these treatments may also be used for other types of BME when necessary. In recent years, extracorporeal shock wave therapy and pulsed electromagnetic fields have also been considered for symptomatic treatment of BME (10). The use of HBOT as a treatment option for BME and related conditions such as bone necrosis is based on the underlying assumption that HBOT may be beneficial in such cases. Nevertheless, it is imperative that scientific evidence substantiates its recommendation as a routine treatment for BME. BME may be associated with limited physiological re-modeling due to reduced bone healing capacity. HBOT has the potential to manage BME by decreasing oxidative stress and pro-inflammatory mediators while increasing the release of growth factors. This may contribute to enhanced healing, improved angiogenesis, and better regulation of vascular tone. (11).

Treatment in BME aims to enhance pain management, improve quality of life, and reduce the duration of the disease. The findings of our study indicate that ten sessions of HBOT led to a significant improvement in the overall quality of life for patients and a notable reduction in pain severity. In a retrospective study focusing on BME in the knee, it was found that patients who received HBOT showed a faster

recovery process compared to those who did not receive treatment. The study involved patients aged 18 to 65 years diagnosed by MRI and treated with a combination of acetylsalicylic acid and bisphosphonates, with some patients receiving HBOT. The study showed a significant improvement in the group that received HBOT, and there were no notable side effects. In this study, patients underwent 30 HBOT sessions (12). The study suggests that 30 sessions of HBOT may be needed to see radiological improvement. However, our research indicates that clinical improvement may begin after just ten sessions of HBOT.

Another study investigated the use of HBOT for BME of the hip. In this prospective, randomized study, two groups were compared: one received pharmacological treatment only, while the other received both pharmacological treatment and 40 sessions of HBOT. The results showed significantly greater BME resolution in the HBOT group, suggesting that HBOT accelerates healing and improves joint function (13). A case report discussed the use of HBOT in treating transient hip osteoporosis. It was confirmed that patients benefited after ten sessions. Additionally, one patient, whose improvement after ten sessions was unsatisfactory, received twenty sessions of HBOT (14). In a study, 18 patients with BME of the hip were followed up for approximately two years after receiving conservative treatment, including HBOT. The study reported that all patients recovered without complications. No significant difference was found between genders in this study. It has been emphasized that an early and accurate diagnosis of hip BME should be made with MRI, and patients can completely recover with conservative treatments (15). Our study observed that the male gender provided more significant improvement in the mean SF-12 general score and mental component after treatment. It is also observed that overweight patients benefit more than normal-weight and obese patients.

Recently, HBOT has been shown to improve cognitive and physical performance in individuals without disease (16-18). This effect may enhance the quality of life for patients. Our study's correlation and regression analyses showed that the enhancement in quality of life was significantly affected by pain levels. This supports the notion that the increased quality of life was linked to improving BME.

Limitations

The study's limitations include retrospective organization, small sample size, lack of long-term follow-up, demographic differences, and the fact that it was conducted in a single center. The implication that ten HBOT sessions in our study are sufficient for BME patients should be avoided. However, the finding that improvement can be observed in ten sessions could serve as a reference for future studies aiming to establish the ideal number of sessions for this disorder.

Conclusion

In conclusion, this study provided valuable insights into the potential of HBOT as an effective treatment for pain-related BME. Findings from our research, which included patients who had previously failed to respond to standard treatments such as immobilization and analgesic-anti-inflammatory drugs, showed that HBOT can significantly improve quality of life and significantly reduce pain intensity. The observation that male patients and those who are overweight may benefit more from HBOT warrants further research to understand the underlying mechanisms contributing to these differences.

The significant negative correlation between post-treatment quality of life scores and pain levels emphasizes the importance of considering HBOT as a promising approach to managing BME, especially in cases where the etiology is unknown. This study provides a basis for future research to confirm these findings and investigate the optimal number of HBOT sessions required for long-term benefits. HBOT is emerging as a viable and promising therapeutic option that can be integrated into the treatment regimen for BME with the potential to improve patient outcomes and quality of life.

Disclosures

Ethical Approval: Ethics committee approval was received for this study from the Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee, in accordance with the World Medical Association Declaration of Helsinki, with the approval number: 2024/125.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - L.D.; Design - L.D., M.Ö.; Supervision - L.D., M.Ö., M.S.I.; Materials - L.D., M.S.I.; Data collection &/or processing - M.A., M.K.; Analysis and/or

interpretation - T.Y.U.; Literature search - M.Ö., M.A., T.Y.U.; Writing - L.D.; Critical review - M.S.I., M.A.

Conflict of Interest: There is no any conflict of interest.

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References

- Baumbach SF, Pfahler V, Bechtold-Dalla Pozza S, Feist-Pagenstert I, Fürmetz J, Baur-Melnyk A, et al. How We Manage Bone Marrow Edema-An Interdisciplinary Approach. *J Clin Med*. 2020; 9:551. <https://doi.org/10.3390/jcm9020551>
- Gosangi B, Mandell JC, Weaver MJ, Uyeda JW, Smith SE, Sodickson AD, et al. Bone Marrow Edema at Dual-Energy CT: A Game Changer in the Emergency Department. *Radiographics*. 2020; 40:859-874. <https://doi.org/10.1148/rq.2020190173>
- Ververidis AN, Paraskevopoulos K, Keskinis A. Bone marrow edema syn-drome/transient osteoporosis of the hip joint and management with the utilization of hy-perbaric oxygen therapy. *J Orthop*. 2020; 22:29-32. <https://doi.org/10.1016/j.jor.2020.03.062>
- Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. *J Clin Epidemiol*. 1998; 51:1171-1178. [https://doi.org/10.1016/S0895-4356\(98\)00109-7](https://doi.org/10.1016/S0895-4356(98)00109-7)
- Soylu C, Kütük B. Reliability and Validity of the Turkish Version of SF-12 Health Sur-vey. *Turk Psikiyatri Derg*. 2022; 33:108-117. <https://doi.org/10.5080/u25700>
- https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form/survey-instrument.html
- Gesoglu DT, Havlioglu S. Pain, health literacy, and related factors in patients with migraine. *Annals Med Res*. 2024;31(6):459-64. <https://doi.org/10.5455/annalsmedres.2024.04.067>
- Boonstra AM, Schiphorst Preuper HR, Balk GA, Stewart RE. Cut-off points for mild, moderate, and severe pain on the visual analogue scale for pain in patients with chronic musculoskeletal pain. *Pain*. 2014; 155:2545-2550. <https://doi.org/10.1016/j.pain.2014.09.014>
- Akhavan S, Martinkovich SC, Kasik C, DeMeo PJ. Bone Marrow Edema, Clinical Sig-nificance, and Treatment Options: A Review. *J Am Acad Orthop Surg*. 2020; 28:e888-e899. <https://doi.org/10.5435/JAAOS-D-20-00142>
- Li S, Yu H, Long S, Li J, He Y, Zheng X, et al. Research Advances in the Treatment of Bone Marrow Edema Syndrome. *J Clin Densitom*. 2023;26:101367. <https://doi.org/10.1016/j.jocd.2023.03.006>
- Capó X, Monserrat-Mesquida M, Quetglas-Llabrés M, Batle JM, Tur JA, Pons A, et al. Hyperbaric Oxygen Therapy Reduces Oxidative Stress and Inflammation, and Increases Growth Factors Favouring the Healing Process of Diabetic Wounds. *Int J Mol Sci*. 2023; 24:7040. <https://doi.org/10.3390/ijms24087040>
- Ozturan B, Akyurek M. Effectiveness of hyperbaric oxygen therapy in bone marrow edemas of the knee: A retrospective study. *Medicine (Baltimore)*. 2023; 102:e33498. <https://doi.org/10.1097/MD.00000000000033498>
- Capone A, Podda D, Ennas F, Iesu C, Casciu L, Civinini R. Hyperbaric oxygen therapy for transient bone marrow oedema syndrome of the hip. *Hip Int*. 2011; 21:211-216.

- <https://doi.org/10.5301/hip.2011.6492>
14. Kesikburun S, Uran A, Demir Y, Transient osteoporosis of the hip and hyperbaric oxygen therapy: A report of two cases. *Turk J Phys Med Rehab.* 2015, 61:80-83.
<https://doi.org/10.5152/tftrd.2015.78055>
 15. Guler O, Ozyurek S, Cakmak S, Isyar M, Mutlu S, Mahirogullari M, et al. Evaluation of results of conservative therapy in patients with transient osteoporosis of hip. *Acta Orthop Belg.* 2015, 81:420-426.
 16. Hadanny A, Daniel-Kotovsky M, Suzin G, Rahav BG, Merav C, Kobi D, et al. Cognitive enhancement of healthy older adults using hyperbaric oxygen: a randomized controlled trial. *Aging.* 2020;12:13740.
<https://doi.org/10.18632/aging.103571>
 17. Hadanny A, Hachmo Y, Rozali D, Catalogna M, Yaakobi E, Sova M, et al. Effects of Hyperbaric Oxygen Therapy on mitochondrial respiration and physical performance in Middle-aged athletes: a Blinded, Randomized Controlled Trial. *Sports Med Open.* 2022;8:22.
<https://doi.org/10.1186/s40798-021-00403-w>
 18. Hadanny A, Sasson E, Copel L, Daniel-Kotovsky M, Yaakobi E, Lang E, et al. Physical enhancement of older adults using hyperbaric oxygen: a randomized controlled trial. *BMC Geriatr.* 2024;24:572.
<https://doi.org/10.1186/s12877-024-05146-3>