Revista Colombiana de Ortopedia y Traumatología
E- ISSN2256 - 490X

ORIGINAL ARTICLE

Characterization of patients with multiple myeloma and spinal cord involvement treated at a tertiary care center in Medellín, Colombia

Caracterización de pacientes con mieloma múltiple y afectación de la columna vertebral atendidos en un hospital de tercer nivel de Medellín, Colombia

Juan José Jaramillo-García[1], Daniela Orrego-Bustamante[1], Eloy Barrios-Henao[2], Damián Martínez-Soto[2,3]

[1] Universidad de Antioquia, Faculty of Medicine, Specialty in Orthopedics and Trauma, Medellín, Colombia.
[2] Universidad de Antioquia, Faculty of Medicine, Medellín, Colombia.
[3] Hospital San Vicente Fundación, Medellín, Colombia.

Open access

Received: 16/06/2021
Accepted: 22/11/2022

Corresponding author: Daniela Orrego-Bustamante, ddaniela.orrego@udea.edu.co.

How to cite: Jaramillo-García JJ, Orrego-Bustamante D, Barrios-Henao E, Martínez-Soto D. Characterization of patients with multiple myeloma and spinal cord involvement treated at a tertiary care center in Medellín, Colombia. Rev Col Or Tra. 2023;37(1):e3. English. doi: https://doi.org/10.58814/01208845.3

Cómo citar: Jaramillo-García JJ, Orrego-Bustamante D, Barrios-Henao E, Martínez-Soto D. [Caracterización de pacientes con mieloma múltiple y afectación de la columna vertebral atendidos en un hospital de tercer nivel de Medellín, Colombia]. Rev Col Or Tra. 2023;37(1):e3. English. doi: https://doi.org/10.58814/01208845.3

Abstract

Introduction: Multiple myeloma (MM) is a type of cancer that originates in plasma cells and can lead to the destruction of bone tissue. Approximately 50% of patients with this condition will experience secondary vertebral fractures.
Objective: To characterize patients with MM and spine cord involvement treated at a tertiary care center.
Methodology: Retrospective, descriptive study conducted using data from patients with MM and spinal cord involvement treated between 2014 and 2018 in a tertiary care center in Medellín, Colombia. Sociodemographic and clinical data were obtained. Quantitative variables are described using means and standard deviations, while qualitative variables are presented as absolute frequencies and percentages with their respective confidence interval (CI95%).
Results: The sample consisted of 109 patients, with a mean age of 63 years and a sex ratio of 1:1. In addition, 78.9% of the participants were newly diagnosed and the most frequent symptom was low back pain (47%). It was also found that an average of 5 sections (vertebral bodies) were affected, that the most frequent method of diagnosis of these lesions was CT scan (62%), and that only 26% of the patients presented with some type of brain lesion. Regarding treatment, 95%, 46%, 55%, and 13% were treated with chemotherapy, radiotherapy, bisphosphonates, and surgery, respectively.
Conclusions: The characteristics of the sample are similar to those reported in other studies, with the exception of sex ratio. Moreover, a low frequency of surgical treatment was observed.
Keywords: Multiple Myeloma; Low Back Pain; Spinal Fractures; Spinal Neoplasia; Pathologic Fracture; Vertebroplasty (MeSH).

Resumen

Introducción: el mieloma múltiple (MM) es un tipo de cáncer que se genera en células plasmáticas y puede provocar la destrucción del tejido óseo. Aproximadamente el 50% de los pacientes con esta enfermedad experimentarán fracturas vertebrales secundarias.
Objetivo: describir las características de pacientes con MM y afectación de la columna vertebral atendidos en un hospital de tercer nivel.
Metodología: estudio descriptivo retrospectivo realizado con los datos de pacientes con MM y afectación de la columna vertebral atendidos entre 2014 y 2018 en un hospital de tercer nivel de atención de Medellín, Colombia. Se obtuvieron datos sociodemográficos y clínicos. Las variables cuantitativas se describen usando medias y desviaciones estándar, mientras que las cualitativas, frecuencias absolutas y porcentajes con su respectivo intervalo de confianza (IC95%).
Resultados: la muestra consistió de 109 pacientes. La edad media fue 63 años, la distribución de sexo fue 1:1, el 78,9% de los participantes fue diagnosticado de novo y el síntoma más frecuente fue dolor lumbar (47%). Además, se encontró una media de 5 niveles (cuerpos vertebrales) afectados, el método de diagnóstico de estas lesiones más frecuente fue la tomografía (62%) y solo el 26% de los pacientes presentaron algún tipo de lesión neurológica. En lo que respecta al tratamiento, 95%, 46%, 55% y 13% fueron tratados con quimioterapia, radioterapia, bifosfonatos e intervención quirúrgica, respectivamente.
Conclusiones: las características de la muestra son similares a las reportadas en otras investigaciones, a excepción de la distribución del sexo. Además, se identificó una baja frecuencia de tratamiento quirúrgico.
Palabras clave: Mieloma múltiple; Dolor lumbar; Fracturas de la columna vertebral; Fractura patológica; Vertebroplastia (DeCS).

Introduction

Multiple myeloma (MM) is a type of cancer that affects plasma cells and is characterized by the excessive growth of neoplastic plasma cells in the bone marrow. This condition can lead to complications related to the destruction of bone tissue, mainly of the spine.[1] In addition, MM is the second most common hematologic cancer after non-Hodgkin's lymphoma, and its annual incidence is six cases per 100 000 inhabitants in Western countries.[2,3]

Vertebral compression fractures have been reported to be the most frequent type of fracture in patients with MM, with a prevalence of between 34% and 64% of cases at disease onset.[4] Despite the burden of morbidity and the impact of these fractures on the quality of life of patients with MM, their radiological characteristics have been poorly described in the literature. It is also presumed that parameters related to the severity of MM are predictive factors for the development of new pathologic fractures.[1] Although recent studies, including Zijlstra *et al.*,[5] have reported that being a female, cancer staging, the presence of low back pain, and changes in bone density visible on computed tomography (CT) are strongly associated with the risk of developing new vertebral fractures, more studies are needed to support these findings.

Few studies have been conducted in the Colombian population diagnosed with MM, for example, some case reports that describe data on patients with this condition in the country.[6,7] However, they do not report information on spinal cord involvement or clinical outcomes in these cases, and no national or regional guidelines have been developed to guide the treatment of patients with this type of cancer. Considering the above and taking into account the increase in the incidence of MM as a result of the increase in life expectancy of the general population, it is important to create guidelines that help to improve the diagnosis and treatment of patients with this condition.

In this sense, it is necessary to characterize the population with MM to have clear information and understand the behavior of this disease in our context, as this may favor the identification of predictive or risk factors for spinal cord involvement and comparisons with international data. Consequently, the aim of this study is to describe the characteristics of patients with multiple myeloma and spinal cord involvement treated at a tertiary care hospital in Medellín, Colombia.

Methodology

Type of study

Retrospective descriptive study.

Population and sample

The study population comprised patients over 18 years of age treated at a tertiary care hospital in Medellín between January 2014 and December 2018 with a diagnosis of symptomatic MM and spinal (cervical, dorsal or lumbar) involvement determined based on imaging tests (x-ray, CT and/or magnetic resonance imaging [MRI]) at the time of MM diagnosis and/or during follow-up. It should be noted that these patients were identified using the International Statistical Classification of Diseases and Related Health Problems (tenth revision [ICD-10]) codes included in the medical records.

Patients were excluded if they had spinal cord involvement of etiology other than MM, patients with a history of spinal fusion or vertebral augmentation procedures (vertebroplasty or kyphoplasty) prior to MM diagnosis, and patients with incomplete

data on the study variables. Considering that the average number of people with MM seen annually at the institution is 30, that approximately 120 patients were treated during the study period (four years), and that 80% of the population with MM has spinal involvement, the minimum sample size for this study was 96 patients.

Procedures

Sociodemographic (age and sex) and clinical data were collected by reviewing electronic medical records. Clinical variables included MM stage (de novo or relapse diagnosis), signs and symptoms at diagnosis, type of neurological lesion, information on imaging tests (imaging test used to define the diagnosis of spinal cord involvement for the first time), affected section of the spine, number of levels (vertebral bodies affected), type of vertebral fracture, presence of lytic lesion in more than 50% of the vertebral body, presence of non-vertebral pathological deformities and presence of non-vertebral pathological fracture, and treatment of MM and spinal involvement. Imaging test results were obtained from the institution's imaging platform.

The characteristics of the imaging tests analyzed were:

- Posterior-anterior and lateral x-ray of the cervical, thoracic or lumbosacral regions of the spine: Presence of fractures; small lytic lesion patterns; mottled or moth-eaten pattern, or large destructive bone lesions in vertebral bodies or posterior elements of the vertebrae.[8]
- CT scan: Presence of distinct fracture patterns, smaller lesions (up to 5mm in trabecular bone) that cannot be visualized on x-ray and bone lacunae. The number of levels (vertebral bodies) affected by a lytic lesion <50% of the vertebral body was established based on the axial and sagittal views of the CT scan and the quantification of each of the affected levels, and/or based on the interpretation stated in the radiology report.[9,10]
- MRI: Since this technique has the highest sensitivity and specificity for evaluating spinal injuries, they were characterized depending on the morphology of vertebral compression fractures and the assessment of the presence of nervous system damage or paraspinal tumors.[11]

Statistical analysis

Quantitative variables are described using means and standard deviations, since the distribution of the data was normal (Kolmogorov-Smirnoff test). Qualitative variables are described using absolute frequencies and percentages.

Ethical considerations

This research followed the ethical principles for conducting biomedical studies involving human subjects established in the Declaration of Helsinki,[12] as well as the scientific, technical, and administrative standards for health research set forth in Resolution 8430 of 1993, issued by the Colombian Ministry of Health.[13] Also, the study was approved by the Research Ethics Committee of the Fundación Hospitalaria San Vicente Paúl by means of Minutes 35-2019 of December 13, 2019. Finally, taking into account that the present study is a retrospective descriptive study in which no additional interventions or procedures were performed on the patients, it was considered to be a low-risk research from an ethical point of view.

Results

A total of 718 patients with a diagnosis of MM and pathologic fractures were identified, of which 109 met *all* inclusion criteria and, consequently, made up the study sample (Figure 1).

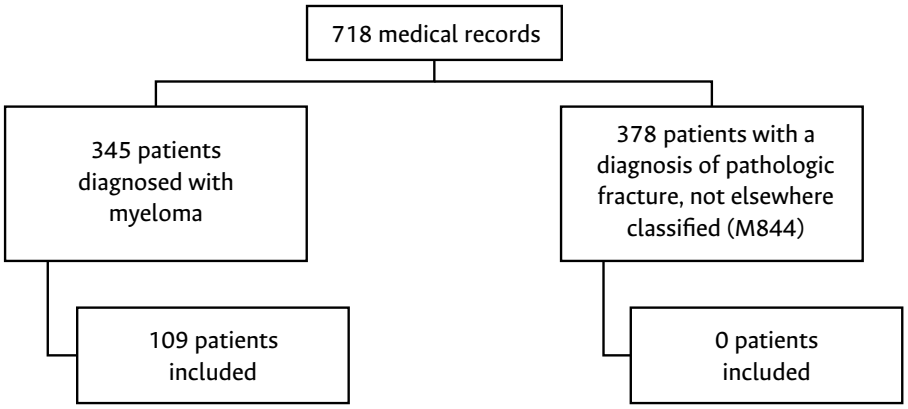

Figure 1. Flow chart of the patients included in the study.
Source: Own elaboration.

In the present study, the mean age was 63.79 years (SD:11.78) and 50.5% were men. Of the patients (n=86), 78.9% were diagnosed de novo and the most frequent symptom was low back pain (46.8%), followed by general malaise (28.4%), bone pain (15.6%), pain in another part of the spine (8.3%), and neurological deficit (0.9%). Furthermore, 26.6% of patients developed some neurological disease, among which the most frequent were compressive myelopathy (17.4%) and radiculopathy (4.6%), and the least frequent were upper limb numbness, transverse myelitis, peripheral neuropathy, sensorimotor polyneuropathy and radiculopathy accompanied by cauda equina, each of these with a prevalence of 0.9% (Table 1).

Table 1. Clinical and sociodemographic findings among the patients included in the study.

	Variable	Frequency (%)
Sex	Male	55 (50.5%)
	Female	54 (49.5 %)
Disease status	De novo diagnosis	86 (78.9 %)
	Relapse	23 (21.1%)
Signs and symptoms at diagnosis	General malaise	31 (28.4%)
	Bone pain	17 (15.6%)
	Low back pain	51 (46.8%)
	Pain elsewhere in the spine	9 (8.3%)
	Neurological deficits	1 (0.9%)
Type of neurological injury	Numbness in upper limbs	1 (0.9%)
	Compressive myelopathy	19 (17.4%)
	Transverse myelitis	1 (0.9%)
	Severe sensory neuropathy	1 (0.9%)
	Sensory-motor polyneuropathy	1 (0.9%)
	Radiculopathy	5 (4,6%)
	Radiculopathy and cauda equina	1 (0,9%)
	None	80 (73,4%)

Source: Own elaboration.

With respect to imaging tests, the most common diagnostic method of spinal lesions was CT scan (62.4%), followed by x-ray, MRI and bone scintigraphy, with a frequency of 19.3%, 13.8%, and 4.6%, respectively. Moreover, the mean number of affected levels was 5 vertebral bodies, 76.1% of patients had lytic lesions in more than 50% of the vertebral body, and 84.4% of patients had vertebral fractures (vertebral compression fracture: 73.4%; wedge-shaped deformity: 5.5%, and vertebral endplate fracture: 5.5%). These injuries were observed in two or more sections of the spine in 73.4% of the cases, while only one section was affected in the other patients, especially in the thoracic vertebrae in 12.8%, the lumbar vertebrae in 11%, the sacrum in 1.8%, and the cervical vertebrae in 0.9%. Finally, it was found that 22% of the patients with vertebral fractures also had a non-vertebral pathologic fracture (Table 2).

Table 2. Imaging findings in the population included in the study.

	Variable	Frequency (%)
Imaging test used to define the diagnosis of spinal cord involvement for the first time	Gammagraphy	5 (4.6%)
	X-ray	21 (19.3%)
	Magnetic resonance imaging	15 (13.8%)
	Computed tomography	68 (62.4%)
Affected spine section	Cervical	1 (0.9%)
	Thoracic	14 (12.8%)
	Lumbar	12 (11%)
	Sacrum	2 (1.8%)
	Two or more sections	80 (73.4%)
Type of vertebral fracture	None	17 (15.6%)
	Vertebral wedge deformity	6 (5.5%)
	End-plate fracture	6 (5.5%)
	Vertebral compression fracture	80 (73.4%)
Lytic lesion in more than 50% of the vertebral body	Yes	83 (76.1%)
	No	26 (23.9%)
Presence of spinal deformities	Increased kyphosis	18 (16.5%)
	Increased lumbar lordosis	4 (3.7%)
	Scoliosis	16 (14.7%)
	Loss of kyphosis	3 (2.6%)
	None	68 (62.4%)
Presence of non-vertebral pathologic fracture	Yes	24 (22%)
	No	85 (78%)

Source: Own elaboration.

Despite the occurrence of lytic lesions in more than 50% of the vertebral body and vertebral fractures, 62.4% of the patients had no spinal deformities. However, it should be noted that in the other patients, the deformities found were increased kyphosis (16.5%), scoliosis (14.7%), increased lumbar lordosis (3.7%), and loss of kyphosis (2.6%) (Table 2).

Regarding MM treatment, 95% of patients received chemotherapy, using steroids (89.9%) and intravenous bisphosphonates (54.1%) as adjuvants (Table 3). Likewise, for the treatment of vertebrae injuries, radiotherapy was performed in 45.9% of the patients and surgical intervention in 12.8%. The most common surgical interventions were vertebroplasty and dorsal spine fixation (3.7% each), while other less frequent procedures included lumbar decompression surgery with dorsal spine fixation, lumbar decompression surgery, laminectomy with lumbar decompression surgery, vertebroplasty with dorsal spine fixation, and paraspinal tumor biopsy.

Table 3. Treatment received by the patients included in the study.

	Variable	Frequency (%)
Chemotherapy	Yes	104 (95.4%)
	No	5(4.6%)
Steroids	Yes	98 (89.9%)
	No	10 (9.2%)
	No information	1 (0.9%)
Bisphosphonate therapy	No	49 (45%)
	Oral	1 (0.9%)
	Intravenous	59 (54.1%)
Radiotherapy	Yes	50 (45.9%)
	No	59 (54.1%)
Spine surgery	No	95 (87.2%)
	Paraspinal tumor biopsy	1 (0.9%)
	Lumbar decompression surgery and dorsal spine fixation	2 (1.8%)
	Lumbar decompression surgery	1 (0.9%)
	Dorsal spine fixation	4 (3.7%)
	Laminectomy and lumbar decompression surgery	1 (0,9%)
	Vertebroplasty	4 (3.7%)
	Vertebroplasty and dorsal spine fixation	1 (0.9%)

Source: Own elaboration.

Discussion

In the present study, the mean age was 63.7 years, which is similar to the age reported in the literature.[14,15] Furthermore, in this study, gender distribution was close to 1:1; however, several studies have reported that the disease is more prevalent in men.[1,2,14] Regarding the diagnosis of MM, most of the patients (78.9%) were diagnosed de novo, thus there is an evident pattern of diagnosis of this disease in advanced stages and in patients with significant spine involvement, resulting in a higher burden of morbidity due to the development of complications. This may be related to the absence of clinical manifestations and symptoms in early stages, as well as to low clinical suspicion. In this sense, it has been reported that, although the symptoms and signs of MM include

anemia, bone disease, hypercalcemia or thrombocytopenia, about 30% of patients with this type of cancer may be asymptomatic, so the presence of MM is only identified after routine medical examinations.

It has been reported that about 80% of patients with MM present with bone involvement[3,11] and that the spine is the most frequently affected site, representing about 60% of the bone lesions found.[6] Besides bone pain, other signs and symptoms are generalized weakness (82%), weight loss (24%), and recurrent bleeding or infections (13%).[3,11] The symptoms reported by the patients in this study are similar to those described by Tossi[2] and Altekruse *et al.*,[11] since low back pain was the most prevalent (46.8%), followed by general discomfort (28.4%), and bone pain (15.6%).

Also, in the present study, 26.6% of the patients developed some neurological disease, most frequently compressive myelopathy (17.4%) or radiculopathy (4.6%). On this matter, it has been reported that spinal cord compression occurs in up to 20% of these patients at various stages of the disease.[4] The pathogenic mechanisms of MM are essentially explained by displacement and mechanical compression in the spinal cord due to tumor invasion into the epidural space, reported in up to 10% of cases, or bone fragments that protrude when the vertebral body is fractured.

The average incidence of vertebral fractures reported is close to 50%,[16] with more than 80% of these fractures occurring in the region between T6 and L4 of the spine and 50% occurring at the thoracolumbar junction, between T11 and L1.[1,15] In the present study, vertebral involvement occurred most frequently in multiple vertebrae (73.4%), and, in particular, 84.4% of patients had vertebral fractures, mainly compression fractures. About this, Lecouvet *et al.*[1] reported that 67% of vertebral compression fractures were benign osteoporotic as per MRI imaging findings, emphasizing that these fractures can be observed both at the time of diagnosis and during treatment. In view of the abovementioned, the presence of MM should be considered as a possibility in patients with acute low back pain and benign-appearing vertebral compression fractures on MRI.

On the other hand, studies in patients with MM[5,8] report the occurrence of spinal deformity as a result of cancer, mainly sagittal imbalance, with an incidence that increases depending on the number of fractures identified at the time of diagnosis. It should be noted that the lumbar and thoracolumbar regions are particularly relevant, since deformity in these areas produces a positive sagittal imbalance.[10] However, there is no established time point at which spinal deformity begins to occur, so it is important to evaluate and prevent it from the beginning of the treatment of patients with MM and spinal cord involvement, especially when patients are diagnosed in advanced stages.[17] In this study, despite the presence of vertebral fractures and lytic lesions in more than 50% of the vertebral body in a significant number of patients, 62.4% of them had no spinal deformities.

It was found that the mean number of affected levels was 5 vertebral bodies, which is similar to the study by Malhotran *et al.*,[10] in which a mean of 3 affected levels was reported. However, there are differences with respect to the treatment given, since Malhotran *et al.*[10] reported that 51% of the cases were treated conservatively and 45% with vertebroplasty, while 87% of the patients in this study received conservative treatment (chemotherapy, steroids, bisphosphonates and/or radiotherapy) and only 12.8% underwent surgery.

Concerning conservative treatments, the use of bisphosphonates has been reported to reduce pain and fracture progression.[18,19] In this study, it was observed that 55% of patients received such treatment. Another conservative treatment strategy is radiotherapy, which aims to reduce pain and the size of the lytic lesion, mainly in patients with

plasmacytomas;[20,21] in this study, radiotherapy was used in 45.9% of the cases found in our setting. Regarding surgical treatments, reports indicate that vertebroplasty in patients with MM helps to reduce the degree of pain and, consequently, improves quality of life.[10,22,23] Taking into account this information and the fact that in this study only 3.7% of the patients received vertebroplasty, it is considered that this therapeutic tool could be used more frequently in the institution.

The limitations of the present study are the lack of information in the medical records, which implies that the data of some patients were not included in the analysis, and the fact that data from only one institution were analyzed, which makes it difficult to generalize or give recommendations on the treatment of patients with MM and spinal cord involvement. Nevertheless, the strength of this study is its sample size, as it is one of the largest in current studies and can be used for future research to create local guidelines for the diagnosis and treatment of patients with MM and spinal cord involvement.

Conclusions

MM is equally common in women and men and is located in the spine in about half of the cases. The most common symptom of this disease is bone pain. Although the lesions caused by MM do not cause major deformities in the vertebral axis, they often lead to chronic pain and secondary neurological injuries. Therefore, timely diagnosis and management of MM with minimally invasive techniques can prevent the onset of these complications.

Conflicts of interest

None stated by the authors.

Funding

None stated by the authors.

Acknowledgments

None stated by the authors.

References

1. Lecouvet FE, Vande Berg BC, Maldague BE, Michaux L, Laterre E, Michaux JL, *et al*. Vertebral compression fractures in multiple myeloma. Part I. Distribution and appearance at MR imaging. Radiology. 1997;204(1):195–9. https://doi.org/jtph.
2. Tosi P. Diagnosis and treatment of bone disease in multiple myeloma: spotlight on spinal involvement. Scientifica (Cairo). 2013:104546. https://doi.org/gb7wcq.
3. Layton KF, Thielen KR, Cloft HJ, Kallmes DF. Acute Vertebral Compression Fractures in Patients with Multiple Myeloma: Evaluation of Vertebral Body Edema Patterns on MR Imaging and the Implications for Vertebroplasty. AJNR Am J Neuroradiol. 2006;27(8):1732-4.
4. Anitha D, Baum T, Kirschke JS, Subburaj K. Risk of vertebral compression fractures in multiple myeloma patients. Medicine (Baltimore). 2017;96(2):e5825.https://doi.org/jtpj.
5. Zijlstra H, Wolterbeek N, Drost RW, Koene HR, Van der Woude HJ, Terpstra WE, *et al*. Identifying predictive factors for vertebral collapse fractures in multiple myeloma patients. Spine J. 2020;20(11):1832-9. https://doi.org/jtn2.

6. Abello V, Idrobo H, Sossa CL, Galvez KM, Saavedra D, Solano MH, et al. The Status of Multiple Myeloma in Colombia: First Report of the Colombian Registry for Hemato-Oncological Diseases (RENEHOC). Asociación Colombiana De Hematologia y Oncologia (ACHO). Blood 2018;132(Suppl 1):5597. https://doi.org/jtpk.
7. Segovia J, Duarte M, Restrepo JG, Saavedra CE, Andrade RE Mieloma múltiple en el Hospital Universitario Fundación Santa Fe de Bogotá (1983-2006). Acta Med Col. 2008;33(4):276-81.
8. Durie BG, Salmon SE. A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. Cancer. 1975;36(3):842–54. https://doi.org/drnxgr.
9. Takasu M, Tani C, Kaichi Y, Yasutaka B, Fujioka C, *et al.* A Longitudinal Study of the Prediction of Pathologic Spinal Fractures in Multiple Myeloma with Trabecular Microarchitecture and CT-Based Finite Element Analyses. J Musculoskelet Disord Treat. 2016;2(3):019.
10. Malhotra K, Butler JS, Ming Yu H. Spinal disease in myeloma: cohort analysis at a specialist spinal surgery centre indicates benefit of early surgical augmentation or bracing. BMC Cancer. 2016;16:444. https://doi.org/f8wb3n.
11. Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W, *et al.* SEER cancer statistics review, 1975–2007 [Internet]. Bethesda, MD: National Cancer Institute; 2010 [cited 2022 Jan 24]. Available from: http://seer.cancer.gov/csr/1975_2007/ index.html.
12. World Medical Association (WMA). WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects. Fortaleza: 64th WMA General Assembly; 2013.
13. Colombia. Ministerio de Salud. Resolución 8430 de 1993 (octubre 4): Por la cual se establecen las normas científicas, técnicas y administrativas para la investigación en salud. Bogotá D.C.; octubre 4 de 1993 [cited 2022 Jan 24]. Available from: https://bit.ly/31gu7do.
14. Terpos E, Roodman GD, Dimopoulos MA. Optimal use of bisphosphonates in patients with multiple myeloma. The American Society of Hematology. Blood. 2013;121(17):3325-8. https://doi.org/jtpm.
15. Brenner H, Gondos A, Pulte D. Recent major improvement in long-term survival of younger patients with multiple myeloma. Blood. 2008;111(5):2521–6. https://doi.org/dnqr44.
16. Gerszten PC, Welch WC. Current surgical management of metastatic spinal disease. Oncology (Williston Park). 2000;14(7):1013– 24.
17. Abello V, Figueroa J, Villamizar L. Mieloma múltiple: clínica, paraclínica y principales esquemas de tratamiento hospital de San José de Bogotá DC. 2003-2010. Repert Med Cir. 2012;21(2):108--14. https://doi.org/jtpn.
18. Dimopoulos M, Terpos E, Comenzo RL, Tosi P, Beksac M, Sezer O, et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple Myeloma. Leukemia. 2009;23:1545-56. https://doi.org/dt9cff.
19. Leigh BR, Kurtts TA, Mack CF, Matzner MB, Shimm DS. Radiation therapy for the palliation of multiple myeloma. Int J Radiat Oncol Biol Phys. 1993;25(5):801–4. https://doi.org/czm6dp.
20. Audat Z, Hajyousef M, Fawareh M, Alawneh KM, Odat MA, Barbarawi MM, et al. Comparison if the addition of multilevel vertebral augmentation to conventional therapy will improve the outcome of patients with multiple myeloma. Scoliosis Spinal Disord. 2016;11:47. https://doi.org/jtpp.
21. Molloy S, Lai M, Pratt G, Ramasamy K, Wilson D, Quraishi N, et al. Optimizing the management of patients with spinal myeloma disease. Br J Haematol. 2015;171(3): 332-43. https://doi.org/f7xfww.
22. Health Quality Ontario. Vertebral augmentation involving vertebroplasty or kyphoplasty for cancer-related vertebral compression fractures: a systematic review. Ont Health Technol Assess Ser. 2016;16(11):1–202
23. Matuschek C, Ochtrop TA, Bölke E, *et al.* Effects of Radiotherapy in the treatment of multiple myeloma: a retrospective analysis of a Single Institution. Radiat Oncol. 2015;10:71. https://doi.org/f67mb9.
24. Pozzi S, Raje N. The Role of Bisphosphonates in Multiple Myeloma: Mechanisms, Side Effects, and the Future. Oncologist. 2011;16(5):651–662. https://doi.org/cpkfp9.