European Journal of Radiology 130 (2020) 109154

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Spectrum of magnetic resonance imaging findings in transplanted multiple myeloma patients with hip/pelvic pain (according to MY-RADS): A single center experience

Federica Rossi[a,b,*], Lorenzo Torri[a], Alida Dominietto[c], Alberto Stefano Tagliafico[a,d]

[a] Department of Health Sciences (DISSAL), University of Genoa, Genova, Italy
[b] Department of Experimental Medicine (DIMES), University of Genoa, Genova, Italy
[c] Second Division of Hematology and Bone Marrow Transplantation, IRCCS AOU San Martino-IST, Genoa, Italy
[d] Department of Radiology, IRCCS San Martino Hospital, Genova, Italy

ARTICLE INFO

Keywords:
Multiple myeloma
Magnetic resonance imaging
Outcomes
Bone marrow

ABSTRACT

Purpose: The aim of our study is to evaluate the spectrum of MRI findings in transplanted Multiple Myeloma (MM) patients with hip/pelvic pain and to correlate these findings with standard prognostic clinical outcomes.
Methods: A retrospective interpretation of the MRI findings of 54 MM patients with hip/pelvic pain were done according to MY-RADS guidelines. MRI findings included: type of bone marrow involvement and incidental findings (osteonecrosis and fractures). Inter- and intra-reader agreement were calculated using Cohen's kappa test. Survival and relapse rates, type of transplantation and days of hospitalization were correlated with MRI findings.
Results: 1/52 patient presented normal bone marrow pattern, 10/52 focal pattern, 26/52 diffuse pattern and 15/52 mixed. No cases of micronodular was reported. Among the incidental findings, n = 6 osteonecrosis and n = 5 pathological fractures were found, with average length of stay higher. The intra- and inter-reader agreement assessing MY-RADS, were good (k value between 0.61 − 0.8). Focal pattern was most represented in patients with osteonecrosis and the worst survival rate. Diffuse pattern was most represented in relapses. No statistically significant correlations were found between bone marrow infiltration patterns and the type of transplantation.
Conclusion: MRI can recognize different infiltration patterns and complications in transplanted MM patients with hip/pelvic pain, correlating with clinical parameters.

1. Introduction

Multiple Myeloma (MM) is the second most common hematological malignant disease and is characterized by autonomous monoclonal proliferation of plasma cells in the bone marrow and by an excessive production of either monoclonal intact immunoglobulin molecules or immunoglobulin free light chains kappa or lambda [1,2]. MM is rare among patients under 40 years of age, but its incidence rises in elderly subjects [3]. Many risk factors are known, including male sex, radiation exposure and monoclonal gammopathy of undetermined significance (MGUS). The normal myeloproliferation is replaced with important clinical impact leading to increasing risk of pathological fractures [3]. In 2003, the International Myeloma Working Group replaced the Durie-Salmon system with a revised version (Durie-Salmon system plus) where the diagnostic role of radiographic is overtaken by the increased sensitivity of Magnetic Resonance Imaging (MRI) and FDG PET/CT in identifying bone marrow involvement [4,5]. MRI has recently become crucial for imaging patients with MM, indeed the Myeloma Response Assessment and Diagnosis System (MY-RADS) was designed to promote standardization in the acquisition, interpretation and reporting of MRI in MM, especially for therapy response assessment [6]. MRI allowed to classify and to quantify bone marrow involvement patterns that is correlated to clinical staging and biopsy [7]. In addition, MRI is a very useful imaging technique to diagnose drug-related complications [8]. Indeed, in MM patients, glucocorticoids are usually administered with chemotherapy to induce high clinical response rates and to relieve some of the side effects of chemotherapy and drugs used in transplant regimes [9]. The cumulative use of systemic corticosteroids is strongly

Abbreviations: MM, multiple myeloma; MGUS, monoclonal gammopathy of undetermined significance; MY-RADS, myeloma response assessment and diagnosis system; FOV, field of view; STIR, shot tau inversion recovery; ESSR, European society of musculoskeletal radiology

* Corresponding author at: Department of Health Sciences (DISSAL), University of Genoa, Genova, Italy.
E-mail address: federossi0590@gmail.com (F. Rossi).

https://doi.org/10.1016/j.ejrad.2020.109154
Received 24 January 2020; Received in revised form 5 May 2020; Accepted 22 June 2020

related to the risk of osteonecrosis of the femoral head. The relationship between osteonecrosis and corticosteroids is thought to be multifactorial resulting from an imbalance in both bone resorption and repair, a compromise of blood supply and bone cell apoptosis [10]. Moreover, osteonecrosis can finally lead to subchondral fractures and femoral head collapse. These complications are very disabling for MM patients who are often compromised [11]. Bone involvement recognition and early identification of therapy complications are crucial to improve clinical outcome and quality of life. Therefore, the aim of our study is to evaluate the spectrum of MRI findings in transplanted MM patients with hip/pelvic pain and to correlate these findings with standard prognostic clinical outcomes.

2. Material and methods

2.1. Patient selection and study design

The retrospective study protocol was approved by our institutional review board (054/2019) and conducted in accordance with the Declaration of Helsinki. A total of n = 54 consecutive MM patients who underwent MRI examination in our university hospital for hip/pelvic pain between January 2017 and December 2019 were included. Inclusion criteria were as follow:

- Patients who had received a diagnosis of MM for which treatment and follow-up were conducted in the hematology department of out university hospital. (n = 95) Among these patients we selected subjects (= 76) treated with hematopoietic cell transplantation (allogeneic or autologous). MM patients treated with hematopoietic cell transplantation (allogeneic or autologous) and corticosteroids who came to our attention for hip/pelvic symptoms (n = 54). The symptoms included prolonged and refractory hip, trochanteric, pubic and pelvic pain; mechanical symptoms such as snapping and clicking of the hip.
- MM transplanted patients with previous osteonecrosis who reported recent ipsilateral or contralateral pain were included.

Exclusion criteria were as follows: inaccurate images due to artifacts (for example metal artifacts in previous hip replacement with arthroplasty), lack of clinical information (incomplete electronic data). Patients affected by other known malignancies were also excluded from the study. Patients with pain coming from other regions (such as back pain radiating or travelling further down the course of nerves) was not considered. Clinical and therapeutical data were collected.

2.2. MRI protocol

MRI was performed on a 1.5-Tesla equipment (Magnetom Avanto, Siemens Healthcare) using a body coil over the pelvis (iliac crest down to midthigh) in supine position (feet first supine). We preferred a 35- to 45-cm FOV (field of view) to evaluate the entire pelvis including the gluteal insertions and trochanteric bursae and to perform a side-to-side comparison of the entire pelvis, even when symptoms are unilateral. According to the literature, the applied MR imaging protocol included standard non-enhanced Turbo Spin Echo (TSE) T1-weighted images and TSE T2-weighted images also with fat saturation or shot tau inversion recovery (STIR), T1-weighted fat-suppressed sequences before and after contrast administration, Diffusion-weighted imaging (DWI) with low, intermediate and high b values and ADC maps [8]. Coronal and axial images represent a minimum examination for most indications; the addition of sagittal images is useful for staging femoral osteonecrosis. Technical inclusion parameters for MRI are reported in Table 1.

2.3. MRI spectrum of findings and statistical analysis

All MRI images were retrospectively evaluated independently by

Table 1
MRI protocol parameters. (Field strength 1.5 T).

Sequences	Repetition Time /Echo Time (TR ms/TE ms)	Slice thickness (mm)	Flip Angle (FA) degree	Respiratory state	Fat Saturation	Field of view (FOV mm)
T1-weighted images (without contrast administration)	476/11	4,5	90	Free	No	400 × 400
T1-weighted images (with contrast administration)	460/10	4	90	Free	Yes	400 × 400
T2-weighted images	2920/59	4,5	150	Free	Yes/No	400 × 400
STIR (shot tau inversion recovery)	2870/31	4,5	150	Free	No	400 × 400
DWI	9800/63	4	90	Free	No	380 × 296,9

Turbo Spin Echo (TSE) T1- and T2- weighted images are used to distinguish cellular from fatty component of bone marrow. STIR (Short tau inversion recovery) determined more homogeneous fat signal suppression than T2-weighted images, but signal-to-noise ratio decreases. T1w are optimally used for depicting anatomic details, while T2w or STIR evaluate the presence of fluid collections and edema within the soft tissue or bone marrow. T1w before contrast administration are used to identify bone marrow malignant infiltration that generally demonstrates avid contrast enhancement (CE). CE can be used to monitor clinical progress and response to therapy. In normal bone marrow, ADC values are generally below 600 – 700 μm^2/sec, instead bone marrow infiltration shows ADC values between 700 – 1400 μm^2/sec). The role of DWI becomes important especially after allogenic stem cell transplantation, when the morphologic identification of focal bone lesions can be obscured for the bone marrow hyperplasia due as a rebound after high-dose therapy or after growth factors.

Table 2
Clinical characteristics of n = 52 MM transplanted patients.

Patients Characteristics	Value
Sex	
Male, (mean age) (y)	28 (53.46 y)
Female, (mean age) (y)	24 (62.83 y)
Age at diagnosis (y), mean ± SD	61.72 ± 14.16
Type of Transplantation	
Autologous	32/52
Allogeneic	20/52
Survival Data	
Death	7/52
Relapse	8/52

two radiologists (A.T and F.R.), subspecialized in diagnostic musculoskeletal imaging, with more than 10 and 5 years of MRI experience, with strong track record of musculoskeletal and myeloma multiple research and European Society of Musculoskeletal Radiology (ESSR) members with Diploma of ESSR (A.T.). The interpretation of the MRI findings was conducted according to MY-RADS guidelines:

1) Pathological bone marrow infiltration patterns on MRI were divided as follow: normal, focal, diffuse, focal on diffuse and micronodular. According to the International Myeloma Working Group, 5 mm was considered as the threshold for focal active lesion. Precise measurements are not possible in lesions less than or equal to 5 mm due to limitations on image resolution. Very small bone marrow lesions were reported for follow-up purposes [6,12].
2) if a soft-tissue disease was incidentally found, it was divided in paramedullary and extra-medullary sites.
3) if vertebral fractures were incidentally found in the field of view (FOV) used for the pelvis/hip, a combination of morphologic and functional imaging were used to characterize the fracture (benign vs malignant).
4) Incidental findings, including osteonecrosis (a complication of MM treatment), pathological fractures or musculoskeletal conditions (acetabular labral tears, abductor disorders and greater trochanteric bursitis, proximal hamstring disorders and ischial bursitis, iliopsoas bursitis, osteochondral and chondral abnormalities in the hip joint, including chondral delamination and ligamentum teres rupture)

We did not evaluate the response assessment category (RAC) as suggest by MY-RADS guidelines, because the aim of our study was to report the spectrum of MRI findings of the hip and pelvis in symptomatic MM transplanted patients [6].

The analysis was performed independently and blindly. Any disagreements were finally resolved by consensus. Any clinical and therapeutic doubts have been solved by the reference hematologist (A.D.), specialized in MM with more than 10 years of experience. A third radiologist (L.T.), who did not evaluate the MRI, created a database to guarantee properly organized data tailored to the present study. A descriptive analysis was performed to quantitatively organize the MRI findings and categorize them.

2.4. Intra- and inter-reader agreement

To promote standardization in the interpretation and reporting MRI findings in MM, MY-RADS guidelines were followed. Inter-reader and intra-reader agreement were evaluated assessing MM imaging findings according to MY-RADS classification using Cohen's kappa test. Reliability coefficients were interpreted, respectively, as poor if less than 0.21, fair if between 0.21 and 0.4, moderate if between 0.41 and 0.6, good if between 0.61 and 0.8, and almost perfect agreement if 0.81–1. Statistical analysis was performed using statistical software [SPSS, version 12.0.1 (SPSS, Inc.); Excel 2007 (Microsoft Corp.]; and STATA MP, StataCorp version 15.0].

2.5. Correlation between MRI findings and clinical data

Survival and relapse rates, type of transplantation and days of hospitalization were determined and correlated with MRI findings.

3. Results

A total of n = 54 consecutive MM patients who underwent MRI examination in our university hospital for hip/pelvic pain between January 2017 and December 2019 were included.According to the study design, a total of 2/54 (3.7 %) MM transplanted patients were excluded, indeed n = 1/2 (50 %) patient had incomplete clinical data (transplant performed in other hospital) and in n = 1/2 (50 %) patient hip pain was caused by degenerative lumbar spinal stenosis. Therefore, a total of n = 52 MM transplanted patients (28 men and 24 women; mean age 65 ± 13 years, range 34–87) was finally included in the study. Of these patients, n = 32/52 (61.54 %) were treated with autologous transplantation and n = 20/52 (38.46 %) with allogeneic transplantation. N = 8/52 (15.38 %) patients experienced relapses. The mean time between the transplantation and the relapse was 1.88 ± 1.36 years. N = 7/52 (13.46 %) patients died during follow-up because of disease progression and complications (e.g. heart disease and infections). Clinical characteristics are summarized in Table 2.

3.1. MRI findings

A total of n = 40/52 (77 %) patients reported at least one pathological imaging finding, in n = 10/52 (20 %) two concomitant pathological imaging findings were diagnosed and in n = 2/52 (3%) patients no pathological imaging finding was demonstrated. No soft-tissue disease (para- or extra-medullary) was incidentally found. No vertebral fractures were incidentally diagnosed.

3.2. Pathological bone marrow infiltration patterns

According to MY-RADS guidelines, n = 1/52 (1.9 %) patient presented normal bone marrow pattern, with high signal intensity on T1-weighted and low signal on T2-weighted images with fat suppression. (Fig. 1) A total of n = 10/52 (19.2 %) focal bone marrow infiltration pattern was found. (Fig. 2) Diffuse bone marrow infiltration was reported in n = 26/52 (52 %) patients. (Fig. 3) Mixed bone marrow infiltration pattern was found in n = 15/52 (28.8 %). (Fig. 4) [13]. No cases of micronodular or "salt and pepper" pattern was reported.

3.3. Incidental findings or drug-related complications

Incidental findings included n = 6 cases of osteonecrosis (Fig. 5) and n = 5 pathological fractures of the femoral head or the hip/pelvis. (Fig. 6) [14,15].

3.4. Intra- and inter-reader agreement

According to Cohen's kappa test, the intra-reader and inter-reader agreement assessing MY-RADS, were considered good (k value between 0.61 − 0.8). Indeed, the intra-reader agreement of radiologist 1 and radiologist 2 were respectively 0.78 and 0.76 and the inter-reader agreement was k = 0.65.

3.5. Correlation between MRI findings and clinical data

Among the 6 patients with osteonecrosis, on MRI, 3/6 (50 %) presented a focal pattern bone marrow involvement, 2/6 (33.3 %) a mixed pattern and 1/6 (16.7 %) a diffuse pattern. Among the 5 patients with pathological fractures, on MRI 3/5 (60 %) had a focal pattern bone

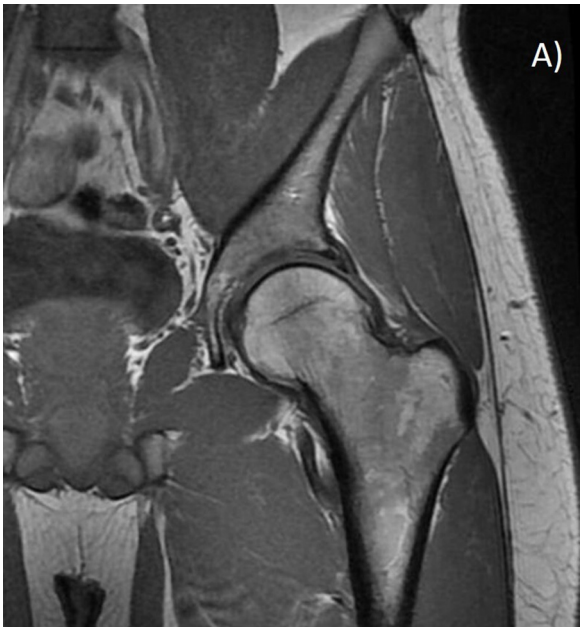

Fig. 1. Normal bone marrow pattern.
In A) axial T1-weighted image of femoroacetabular joint with fatty bone marrow characterized by intermediate-high signal intensity.

marrow involvement and 2/5 (40 %) a mixed pattern. Table 3 summarized the data found. The average length of stay in hospital was higher in patients who experienced complications such as osteonecrosis and pathological fractures (average length of stay: 12.25 days versus 2.21 days). The patients who presented the worst survival rate was the group with a focal pattern (70 %) followed by a mixed pattern (86.67 %) and a diffuse pattern (92.31 %) (Table 4). Among the patients who died (7/52, 13.46 %) during follow-up, 3/7 (42.86 %) had a focal pattern, 2/7 (28.57 %) had a diffuse and mixed pattern. Among the patients who had relapses (8/52, 15.38 %), 4/8 (50 %) had a diffuse pattern, 3/8 (37.5 %) a mixed pattern and 1/8 (12.5 %) a focal pattern. No statistically significant correlations were found between bone marrow infiltration patterns and the type of transplantation.

4. Discussion

In the diagnostic pathway of MM, MRI is recognized as an important and fast method that can be used in daily clinical practice. Bone involvement recognition and early identification are crucial to improve clinical outcome and quality of life of MM patients. MRI can recognize five different patterns of bone marrow involvement in MM: normal, focal (with lesion of diameter 5 mm), diffuse, combined diffuse and focal and micronodular [12].

In the Durie-Salmon PLUS system, the number of focal lesions is used for the staging of MM patients [12]. Several studies evaluated the number of symptomatic MM patients with each of the abnormal MRI bone marrow involvement pattern, reporting a percentage of 10 % for focal pattern, 28 % for diffuse, and 40 % for mixed and 22 % for minimal [16]. However, the percentages seem to vary in different studies, probably due to the different classification systems used. According to MY-RADS, we found a percentage of 192% focal pattern, 52 % of diffuse and 288% of mixed. The difference in results could be partly explained by the fact that we made an exclusive evaluation of the hip/pelvis whereas the other studies have mostly done a total body MRI evaluation.

Previous studies reported that MRI findings correlated with histopathological data [7]. In addition, bone marrow patterns on MRI can provide prognostic information for patients with MM [15].

The hip/pelvis seem to be particularly affected by both the primary disease and therapy-related complications (especially glucocorticoids, widely used in MM patients). Glucocorticoids reduce blood flow to the affected bone and osteonecrosis of the femoral head is thought to be a result of impeded blood supply causing death of osteocytes. Indeed, the cumulative use of systemic corticosteroids is strongly related to the risk of osteonecrosis and fractures of the femoral head [9]. MRI is considered the most propitious technique in the investigation of femoral osteonecrosis and drives management decision-making.

According with previous literature, the focal pattern showed the worst survival rate [15,17,19]. In our study, the worst survival rate was found in patients with a focal pattern (70 %) followed by a mixed pattern (86.67 %) and a diffuse pattern (92.31 %), as reported in the literature [15,17,19]. Among the patients who died (13.46 %) during follow-up, 42.86 % had a focal pattern, 28.57 % had a diffuse and mixed pattern. The presence of large focal lesions is a strong independent prognostic factor in multiple myeloma. Indeed, focal pattern seems to be a dominant pattern associated with more aggressive disease (shorter progression-free survival) [17,18]. In the recent study, Tagliafico et al. reported worst prognostic outcome in MM patients with focal pattern evaluating with a Radiomics approach focal lesions on CT [19]. In addition, the results of our study showed that the focal pattern was the most representative bone marrow involvement among the patients with osteonecrosis (6/52) and pathological fractures of the femoral head (5/52). Moreover, patients with osteonecrosis and pathological fractures reported higher average length of stay in hospital. Focal pattern may represent purely lytic bone lesions with increased local osteoclast activity and suppressed new bone formation by osteoblasts.

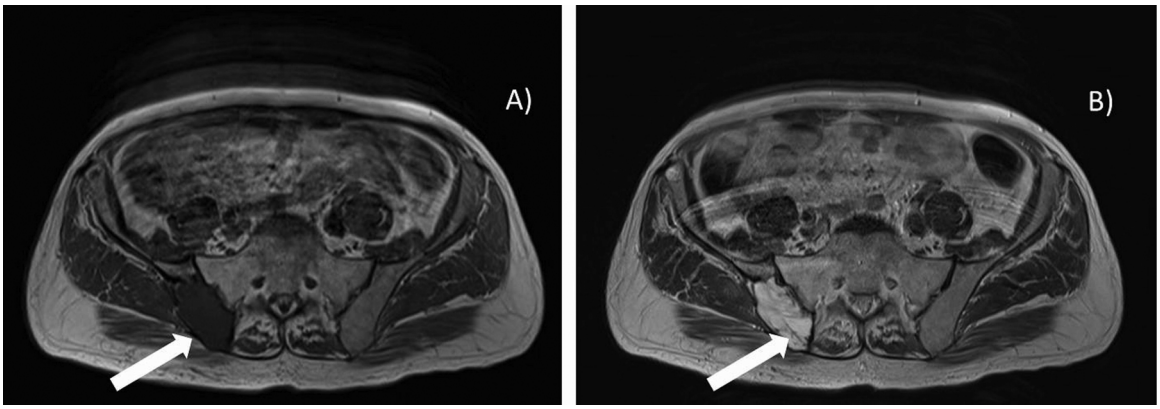

Fig. 2. Example of focal bone marrow infiltration pattern.
In A) axial T1-weighted image of a sacroiliac joint with a focal typically hypointense lesion at the level of the right iliac bone (white arrow). In B) axial T2-weighted image of the same focal lesion, characterized by high signal intensity.

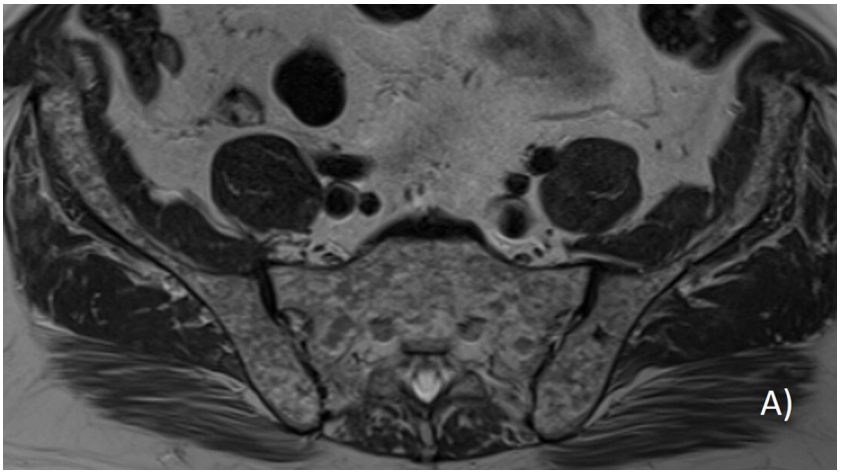

Fig. 3. Example of diffuse bone marrow infiltration pattern.
In A) an axial T1-weighted image showed diffuse bone marrow infiltration pattern, with a typical homogenous decrease of signal.

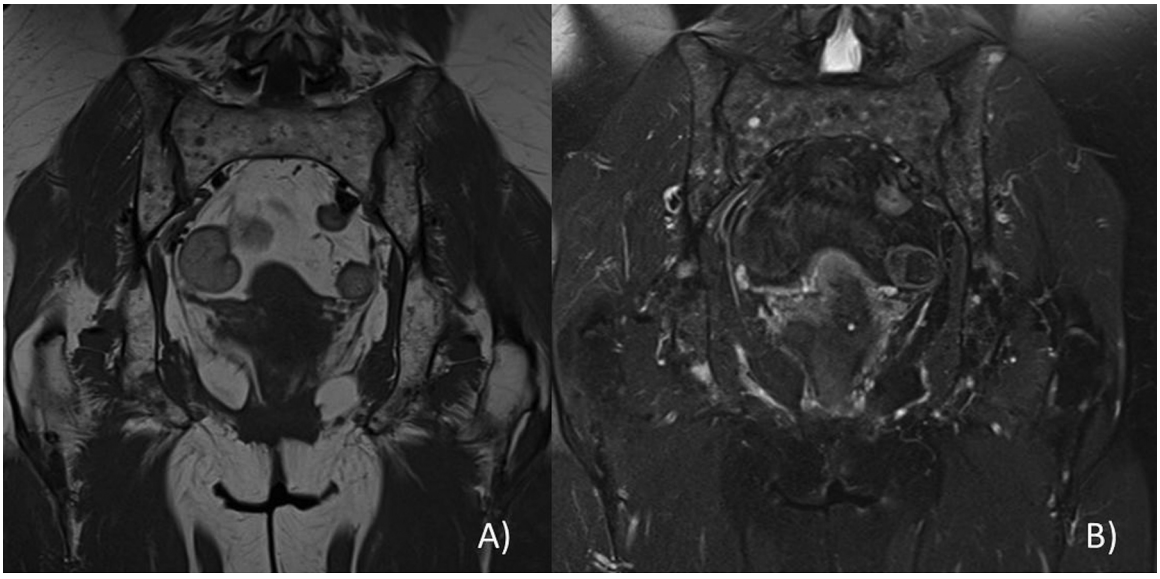

Fig. 4. Example of mixed bone marrow infiltration pattern.
In this combined pattern, on coronalT1-weighted image (A), the bone marrow at the level of the hip shows a diffusely decreased signal intensity with additional focal lesions interspersed, that are better demarcated on coronal fat-suppressed T2-weighted sequences.

The aim of our study was to evaluate the spectrum of MRI findings in transplanted MM patients with hip/pelvic pain and to correlate these findings with prognostic clinical outcomes. This study compared, for the first time to our knowledge, the risk of osteonecrosis of the femoral head and hip/femur fractures with the different pattern of bone marrow involvement in MM patients. The results suggested the possible prognostic value of focal pattern detected by MRI in patients with MM for progression into therapy side-effect. MRI could help in the early detection of osteonecrosis in MM patients with focal pattern and may allow treatment regimen modification and regular MRI monitoring. To the best of our knowledge, this is the first study that followed MY-RADS guidelines with a good intra- and inter-reader agreement in the interpretation and reporting MRI findings, even if the response assessment categories were not evaluated for study purposes.

Several limitations of our study need to be acknowledged. A known limitation is the retrospective nature of the study and the relative low number patients when divided in subgroups that did not allow relative risk and odds ratio calculations for each variable. In addition, we did not correlate MRI findings according to international staging system (e.g. Durie and Salmon Plus system) as previously done [15]. The data of the present study could be considered to promote further larger multicentric studies with a bigger sample size to define the risk of relapse or death and the risk of side effects (such as osteonecrosis) associated with a focal pattern

5. Conclusions

In conclusion, this study described a wide spectrum of magnetic resonance imaging findings, infiltration patterns and complications, in transplanted multiple myeloma patients with hip/pelvic pain and correlated MRI findings with clinical parameters. The presence of focal lesions seemed to correlate with both significant adverse prognostic factors and risk of treatment side-effect for patients with MM.

CRediT authorship contribution statement

Federica Rossi: Conceptualization, Validation, Resources, Data curation, Writing - original draft, Writing - review & editing. **Lorenzo Torri:** Resources, Data curation, Visualization. **Alida Dominietto:** Validation, Formal analysis, Supervision. **Alberto Stefano Tagliafico:**

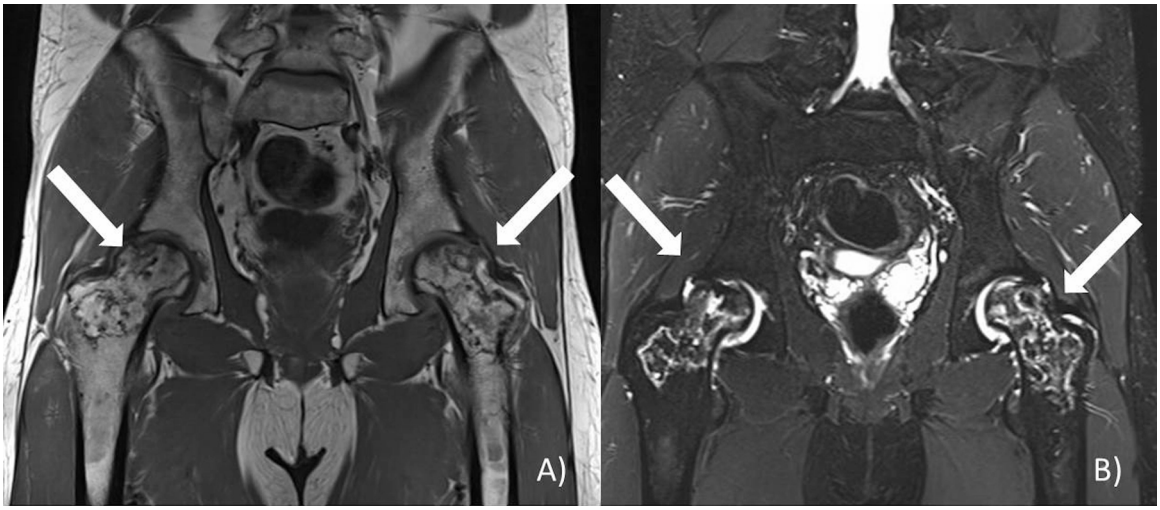

Fig. 5. Example of osteonecrosis of the femoral head.
In femoral head osteonecrosis, coronal T1-weighted image showed areas of low signal due to edema bordered by a hyper-intense line due to blood products (white arrows in A), instead the "double line sign" consisting of a low signal intensity outer rim and high signal intensity inner line is demonstrated on coronal T2-weighted image (white arrows in B).

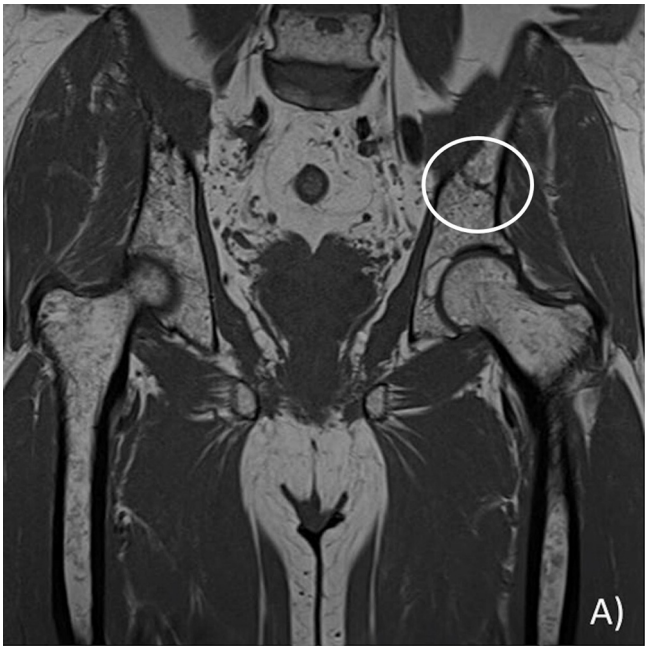

Fig. 6. Example of hip fracture.
In A) a coronal T1-weighted image showed a fracture of the left iliac bone in a transplanted MM patient with a mixed pattern of bone marrow involvement. The iliac fracture is seen as a linear almost horizontal line (white circle).

Project administration, Supervision, Writing - original draft, Conceptualization.

Declaration of Competing Interest

None.

Acknowledgement

None.

Table 3
a summary view of the data obtained.

MRI findings: Pattern of bone marrow involvement	Number of patients (total = 52)
1) Normal pattern	1
2) Focal pattern	10
3) Diffuse pattern	26
4) Mixed pattern	15
5) Micronodular pattern	0
MRI incidental findings	
Osteonecrosis of the femoral head:	6
- focal pattern	3/6
- mixed pattern	2/6
- diffuse pattern	1/6
Femoral head fracture	5
- focal pattern	3/5
-mixed pattern	2/5

Table 4
Overall Survival Rate According to Different MRI bone marrow infiltration patterns.

MRI bone marrow infiltration pattern	No. of Patients	No. of Patients Alive at the end of Follow-up	Overall Survival Rate (%)
Focal	10	7	70
Diffuse	26	24	92.31
Mixed	15	13	86.67
Normal	1	1	100

References

[1] T. Derlin, P. Bannas, Imaging of multiple myeloma: current concepts, World J. Orthop. (2014) 272–282, https://doi.org/10.5312/wjo.v5.i3.272.
[2] E. Zamagni, C. Nanni, K. Mancuso, P. Tacchetti, A. Pezzi, L. Pantani, et al., PET/ CT improves the definition of complete response and allows to detect otherwise unidentifiable skeletal progression in multiple myeloma, Clin. Cancer Res. (2015) 4384–4390, https://doi.org/10.1158/1078-0432.CCR-15-0396.
[3] A. Stecco, F. Buemi, A. Iannessi, A. Carriero, A. Gallamini, Current concepts in tumor imaging with whole-body MRI with diffusion imaging (WB-MRI-DWI) in multiple myeloma and lymphoma, Leuk. Lymphoma (2018) 2546–2556, https://doi.org/10.1080/10428194.2018.1434881.
[4] K. Fechtner, J. Hillengass, S. Delorme, C. Heiss, K. Neben, H. Goldschmidt, H.U. Kauczor, M.A. Weber, Staging monoclonal plasma cell disease: comparison of the durie-salmon and the durie-salmon PLUS staging systems, Radiology (2010) 195–204, https://doi.org/10.1148/radiol.10091809.

[5] M. Cavo, E. Terpos, C. Nanni, P. Moreau, S. Lentzsch, S. Zweegman, et al., Role of ^{18}F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group, Lancet Oncol. (2017) e206–e217, https://doi.org/10.1016/S1470-2045(17)30189-4.

[6] C. Messiou, J. Hillengass, S. Dedorme, F.E. Lecouvet, L.A. Moulopoulos, D.J. Collins, et al., Guidelines for acquisition, interpretation, and reporting of whole-body MRI in myeloma: myeloma response assessment and diagnosis system (MY-RADS), Radiology (2019) 5–13, https://doi.org/10.1148/radiol.2019181949.

[7] A. Stäbler, A. Baur, R. Bartl, R. Munker, R. Lamerz, M.F. Reiser, Contrast enhancement and quantitative signal analysis in MR imaging of multiple myeloma: assessment of focal and diffuse growth patterns in marrow correlated with biopsies and survival rates, AJR Am. J. Roentgenol. (1996) 1029–1036, https://doi.org/10.2214/ajr.167.4.8819407.

[8] S.M. Navarro, G.R. Matcuk, D.B. Patel, M. Skalski, E.A. White, A. Tomasian, et al., Musculoskeletal imaging findings of hematologic malignancies, Radiographics (2017) 881–900, https://doi.org/10.1148/rg.2017160133.

[9] N. Burwick, S. Sharma, Glucocorticoids in multiple myeloma: past, present, and future, Ann. Hematol. (2019) 19–28, https://doi.org/10.1007/s00277-018-3465-8.

[10] K.L. Gebhard, H.I. Maibach, Relationship between systemic corticosteroids and osteonecrosis, Am. J. Clin. Dermatol. (2001) 377–388, https://doi.org/10.2165/00128071-200102060-00004.

[11] K. Stevens, C. Tao, S.U. Lee, N. Salem, J. Vandevenne, C. Cheng, et al., Subchondral fractures in osteonecrosis of the femoral head: comparison of radiography, CT, and MR imaging, AJR Am. J. Roentgenol. (2003) 363–368, https://doi.org/10.2214/ajr.180.2.1800363.

[12] M.A. Dimopoulos, J. Hillengass, S. Usmani, E. Zamagni, S. Lentzsch, F.E. Davies, et al., Role of magnetic resonance imaging in the management of patients with multiple myeloma: a consensus statement, J. Clin. Oncol. (2015) 657–664, https://doi.org/10.1200/JCO.2014.57.9961.

[13] J.C. Dutoit, K.L. Verstraete, MRI in multiple myeloma: a pictorial review of diagnostic and post-treatment findings, Insights Imaging (2016) 553–569, https://doi.org/10.1007/s13244-016-0492-7.

[14] M.F. Glickstein, D.L. Burk Jr., M.L. Schiebler, E.K. Cohen, M.K. Dalinka, M.E. Steinberg, H.Y. Kressl, Avascular necrosis versus other diseases of the hip: sensitivity of MR imaging, Radiology (1988) 213–215, https://doi.org/10.1148/radiology.169.1.3420260.

[15] G. Filonzi, K. Mancuso, E. Zamagni, C. Nanni, P. Spinnato, M. Cavo, et al., A comparison of different staging systems for multiple myeloma, AJR Am. J. Roentgenol. (2017) 152–158, https://doi.org/10.2214/AJR.16.17219.

[16] M. Andrulis, T. Bäuerle, H. Goldschmidt, O. Landgren, P. Schirmacher, J. Hillengass, Infiltration patterns in monoclonal plasma cell disorders: correlation of magnetic resonance imaging with matched bone marrow histology, Eur. J. Radiol. (2014) 970–974, https://doi.org/10.1016/j.ejrad.2014.03.005.

[17] J. Hillengass, K. Fechtner, M.-A. Weber, T. Bäuerle, S. Ayyaz, C. Heiss, T. Hielscher, T.M. Moehler, G. Egerer, K. Neben, A.D. Ho, H.U. Kauczor, S. Delorme, H. Goldschmidt, Prognostic significance of focal lesions in whole-body magnetic resonance imaging in patients with asymptomatic multiple myeloma, J. Clin. Oncol. (2010) 1606–1610, https://doi.org/10.1200/JCO.2009.25.5356.

[18] A. Baur, A. Stabler, D. Nagel, R. Lamerz, R. Bartl, E. Hiller, et al., Magnetic resonance imaging as a supplement for clinical staging system of Durie and Salmon, Cancer (2002) 1334–1345, https://doi.org/10.1002/cncr.10818.

[19] A.S. Tagliafico, M. Cea, F. Rossi, F. Valdora, B. Bignotti, G. Succio, et al., Differentiating diffuse from focal pattern on Computed Tomography in multiple myeloma: added value of a Radiomics approach, Eur. J. Radiol. (2019), https://doi.org/10.1016/j.ejrad.2019.108739.