Osteoporosis in male patients: epidemiology, clinical aspects and DEXA Scan assessment

Michele Bisaccia¹
Giuseppe Rinonapoli¹
Luigi Meccariello²
Umberto Ripani³
Valerio Pace¹
Giuseppe Rollo²
Cristina Ibáñez-Vicente⁴
Olga Bisaccia⁵
David Gómez-Garrido⁶
Miguel Carrato-Gómez⁷
Sandra Guijarro-Leo⁷
Auro Caraffa¹
Alessandra De Masi De Luca⁸

¹ Trauma & Orthopaedic Department, “S.M. della Misericordia” Hospital, University of Perugia, Perugia, Italy
² Department of Orthopedics and Traumatology, “Vito Fazzi” Hospital, Lecce, Italy
³ Division of Anesthesia, Analgesia and Intensive Care and Pain Therapy, Department of Emergency and Major Trauma, “Ospedali Riuniti di Ancona”, Ancona, Italy
⁴ Department of Internal Medicine, Hospital de Getafe, Spain
⁵ Department of Radiology, Hospital “San Carlo”, Potenza, Italy
⁶ Department of Orthopaedics and Traumatology, Orthopaedic and Traumatology Unit, Hospital Quirón Salud Toledo and Hospital Solimat Toledo, Spain
⁷ Department of Orthopaedic and Traumatology, “Complejo Hospitalario Universitario de Toledo”, Toledo, Spain
⁸ Department of Rehabilitation Medicine, “Cardinale Panico” Hospital, Tricase (LE), Italy

Address for correspondence:
Luigi Meccariello
Department of Orthopedics and Traumatology
Vito Fazzi Hospital
Piazzetta Filippo Muratore, Block: A- Floor:V
Lecce, Italy
E-mail: drlordmec@gmail.com

Summary

Introduction. Osteoporosis in male patients affects a significant number of the overall population and is the cause of a relevant percentage of fragility fractures. Our aim: to describe the epidemiology, clinical aspects and DEXA Scan assessment and results of osteoporosis in male patients at one single specialist center. Materials and methods. Retrospective study. All DEXA Scans performed at one single specialist center within the set time-frame of one year were selected. We sub-selected scans belonging to male patients older than 18 years. The Z-score was for patients with an age between 18 and 50. A standard deviation bigger than -2.5 was considered as diagnosis of osteoporosis for the first group, while a standard deviation bigger than -2.0 and history of osteoporotic fracture was again considered as diagnosis of osteoporosis in the second group.

Results. Among the overall 4369 performed scans, 376 (8.6%) matched the including criteria. Among those, 129 (of which 78% aged older than 50) had abnormal scan results. Mean age: 60 ± 13. BMI: 25.5 ± 2.8 kg/m². 61 patients were diagnosed with osteoporosis according to scan results and the rest sustained an osteoporotic fracture. Densitometric osteoporosis: 49% spine, 33% hip, 18% spine and hip. 30 of the 61 patients had history of osteoporotic fracture of the spine, hip, wrist or other sites. 21% of these 30 patients was older than 50.

Conclusions. Osteoporosis in males must be considered a serious disease. 1 in 6 of the included patients had diagnosis of osteoporosis. We would like to highlight the importance of osteoporosis in males and to improve early diagnosis, prevention and treatments, especially among high risk patients.

KEY WORDS: osteoporosis in males; DEXA Scan; T-Score; Z-Score; fragility fracture; body mass density.

Introduction

Osteoporosis in male patients affects a significant number of the overall population and is the cause of a relevant percentage of fragility fractures. This percentage is gradually increasing over the last few years. About 20% of patients older than 50 have a diagnosis of osteoporosis. About one third of overall fractures in males are caused by osteoporosis. The related morbidity and mortality of this population is three times higher than the female population (1-3). The diagnosis of osteoporosis is based on the presence of fragility fractures (spontaneous fractures not caused by high energy trauma or caused by low energy trauma) and/or considering values obtained with the performance of DEXA Scans following the criteria of the International Society for Densitometry Clinical (ISCD). However the T-score is not needed for patients under investigation of osteoporosis if the score is less than -2.5. Differently the T-score is recommended for male patients older than 50 in order to diagnose osteoporosis with scores of -2.5 DS (similarly to what happened for female patients) (4-7).

For males younger than 50 it is suggested to utilize the Z-score for the assessment of BMD, considering as normal values of >-2.0 DS. BMD values < -2.0 DS are considered as low bone mass in relation to age and gender and are not diagnostic for osteoporosis in absence of a fragility fracture or multiple risk factors for osteoporosis (use of steroids, hypogonadism, etc.) (8, 9).
Osteoporosis in male patients has a secondary cause in 50% of the overall cases. Differently osteoporosis in post-menopause female patients has a secondary cause in about 20-30% of the cases. In absence of a clearly identifiable primary or secondary cause, osteoporosis is defined as idiopathic in male patients in the range of age between 30 and 70 years (10, 11). The aim of this study is to describe the epidemiology, clinical aspects and DEXA Scan assessment and results of osteoporosis in male patients managed at one single specialist center in order to improve early diagnosis, prevention and treatments, especially among high risk patients.

Materials and methods

Retrospective study including all DEXA Scans performed at one single specialist center within the set time-frame of one year. 4369 Scans were performed over the selected time-frame. Mean age: 60 ± 13. BMI: 25.5 ± 2.8 kg /m². Inclusion criteria: all DEXA Scans performed between January 2015 and January 2016 at one single specialist center belonging to male patients older than 18. Hologic QDR 4500 A (HOLOGIC, INC. North and South America, Pacific Rim 35 Crosby Drive, Bedford, MA) was the utilized Scan machine. Availability of pre and post-scan medical information (epidemiology, etiology, comorbidities, sustained fractures, ongoing or previous treatments) and radiological investigations to be reviewed for the purpose of our study. Exclusion criteria: DEXA Scans belonging to female patients or male patients younger than 18, DEXA Scans outside the set time-frame. Patients with insufficient pre and post-scan medical and radiological documentation. 4369 DEXA Scans were overall performed in the set time-frame. We sub-selected scans belonging to male patients older than 18 years. The T-score was utilized for patients older than 50, and the Z-score for patients with an age between 18 and 50. A standard deviation bigger than -2.5 (among patients and mean value recorded within the healthy population) was considered as diagnosis of osteoporosis for the first group, while a standard deviation bigger than -2.0 (among mean value recorded within the healthy male population and patient) and history of osteoporotic fracture was again considered as diagnosis of osteoporosis in the second group.

The selected included patients with abnormal DEXA Scan results were clinically examined. The relevant medical and radiological documentation was also reviewed. The following clinical data were collected: anthropometric parameters at the time of diagnosis (weight, height), lifestyle aspects (alcohol, smoke, drugs, milk consumption, sport activities), type of osteoporosis diagnosis (idiopathic or secondary), diagnosis made following DEXA Scans or secondary to fragility fracture, treatments. The DEXA Scan machine set-up and his calibration was kept unchanged throughout the entire duration of the study. All patients were informed in a clear and comprehensive way about all implications of a diagnosis of osteoporosis and his treatments and involvement in the study. Patients were treated according to the ethical standards of the Helsinki Declaration, and were invited to read, understand, and sign an informed consent form.

Treatments for patients diagnosed with osteoporosis were as follows: calcium for 62% of the patients, vitamin D for 50%, bisphosphonates for 45%, androgen hormones for 4%. 5.9% of the overall patients did not have any pharmacological treatment.

Results

4369 DEXA Scans were performed over the studied period of time. Among these, 376 (8.6%) matched the including criteria. Among these, 129 (of which 78% aged older than 50) had abnormal scan results. Mean age: 60 ±13. BMI: 25.5 ± 2.8 kg /m². 61 patients were diagnosed with osteoporosis according to scan results and the rest sustained an osteoporotic fracture. The mean age of the studied population (376 male patients with age > 50) was 60 ± 13 (range 18 to 87 years). Mean BMI was 25.5 ± 2.8 kg /m² (lower value was 20.5 kg /m² and higher value was 31.7 kg/m²) (Table 1).

Table 1 - Simple description of the population.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>376</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
</tr>
<tr>
<td>Breed</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Average age</td>
<td>60 ± 13 years</td>
</tr>
<tr>
<td>Average BMI</td>
<td>25.5 ± 2.8 kg /m²</td>
</tr>
</tbody>
</table>

DEXA Scans results for the studied population were reviewed and ISCD criteria (International Society for Clinical Densitometry) were used for results analysis. 129 patients (34.3%) had normal DEXA values (78% of these patients was older than 50). 61 out of 129 patients with normal DEXA values (47.2%) had diagnosis of osteoporosis. 64% of these diagnosis were made following abnormal DEXA results, while the rest (36%) of the diagnosis were made following low bone mass density values in association with fragility fractures.

Out of the patients with densitometric osteoporosis, 49% had his spine (vertebrae) involved, 33% had his hips involved and finally 18% had both sites involved. 30 of the 61 patients (49.1%) had history of osteoporotic fracture (vertebrae, hip, wrist or other less common sites involved). 21% of these patients was older than 50. Causes of osteoporosis were as follows: 24% idiopathic, 18% related to steroids, 19% related to lack of vitamin D, 16% related to chronic renal insufficiency.

30 out of the 61 patients (49.1%) sustained a fragility fracture with the following cut-off for anatomical site involved: 58% spine, 13% hip, 7% wrist and 22% other sites (Figure 1). 71% of these 30 patients were older than 50. Causes of osteoporosis among these patients were as follows: 24% idiopathic, 21% related to steroids, 17% related to lack of vitamin D, 15% related to chronic renal insufficiency.

With regards to alimentary habits of the studied cases, a significant consumption of milk derived products was highlighted in 12 patients, with a mean daily consumption of 1.4 litters. 33 patients revealed to regularly smoke tobacco 9 patients regularly drink alcohol. 49.1% (30) of the patients claimed to regularly exercise at least 2 times a week (15 were runners, 10 went to the gym, 2 played non competitive soccer and 3 played non competitive tennis).
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Treatments for patients diagnosed with osteoporosis were as follows: calcium for 62% of the patients, vitamin D for 50%, bisphosphonates for 45%, androgen hormones for 4%. 5.9% of the overall patients did not have any pharmacological treatment.

Discussion

The increasing aging of the overall population is a progressive emerging global health problem, affecting mostly women (male:female 1:4). Only about 1 quarter of the diagnosed cases of osteoporosis are males. Osteoporosis in women is considered a quite disabling as it can cause fractures due to weaker bones, particularly in the post-menopause period. These fractures are commonly named fragility fractures. After the age of 50, 1 women out of 3 sustained a fragility fracture (1 out of 5 for men). These discrepancy in terms of epidemiology numbers justify the presence of a rich literature on osteoporosis in women and a lack of studies with regards to men. However more depth into male osteoporosis should be considered a global public health as well, given the overall big numbers. About 20% of overall femur fractures are sustained by males. While the incidence of fragility fractures is higher in females, morbidity and mortality are higher in male patients (2, 10-13).

Another major difference about osteoporosis in males and females is that it is considered more frequently a secondary pathology in males than in females (2/3 in males against 1/3 in females). Therefore Authors must pay big attention to taking into account all conditions that could possibly cause secondary osteoporosis. More common secondary causes are: hypogonadism, alcohol consumption, multiple myeloma, hyperparathyroidism, malabsorption, use of steroids (14, 15).

Recent studies have shown that 11% of males older than 70 with high BMI (body mass index) had neck of femur osteoporosis; this is an element in favour of relevancy of BMI in osteoporosis ethiology. Prevalence of adult fractures (independently from the ethiology) has been shown to be higher in males than females (22.4% in males against 13.7% in females); prevalence is higher in the female group exclusively in the subgroup formed by the population older than 65 (30.5% in females against 24.1% in males). This could be justified by the fact that osteoporosis is more common (and with increasing prevalence) in the older subgroups of population, while fractures in younger individuals are more commonly related to work or sports (more commonly practised by men) (16, 17).

A DEXA Scan is a useful investigation for the purpose of clarity among doubtful diagnosis of osteoporosis in males with previously sustained fragility fractures. This investigation is also the imaging of choice for the evaluation of bony mass and risk of fractures in males with no sustained fracture at risk of osteoporosis. Moreover a DEXA Scan is clinically justified for the evaluation of the bony mass of males of any age if in presence of a major risk factor (e.g. fragility fracture, steroids, etc.). It is also recommended in any individuals between the age of 50 and 69 in presence of 2 or more minor risk factors. Risk factors do not vary among male and female patients (family history, fragility fractures, medications such as steroids, pathologies causing reduction of bone mass among the most common) (18, 19).

Several national guidelines (e.g. American and English guidelines) consider the execution of DEXA Scans cost-effective only for patients older than 70. Densitometric criteria for the diagnosis of osteoporosis do not differ among male and female patients but a discrepancy should be highlighted in terms of level of evidence, as it is lower for males (20). The diagnostic cut-off currently used for the diagnosis of osteoporosis is a T-score < -2.5 DS of adult males compared to young males. With regards to the use of Ultrasound Scans (QUS) for the diagnosis of osteoporosis, data obtained from the male population are similar to those obtained in the female population. Results are however still inconclusive and anyway not definitive. In fact the use of QUS is not recommended either for males and females. In over than 50 years old males a plain radiograph of the spine is always the commonest.

Figure 1 - Description of fracture site. Spine is always the commonest.
thoracic-lumbar tract of the spine is suggested in order to
evaluate the presence of compression fractures, especially
in patients with history of fragility fractures, loss of height
bigger than 4 cm (compared to the height recorded 20 years
before) or ongoing/previous steroids treatments. Same ra-
diographs are also suggested in males between the age of
70 and 79 if T-score (vertebral or femoral) < -1.5, or above
the age of 80 if T-score < -1 (21, 22).

In our study more than one third of the men who underwent
a DEXA Scan was revealed to have a relevant degree of
BMD reduction and about 1 in 6 men had diagnosis of os-
teoporosis after the execution of a DEXA Scan. In half of
our patients with diagnosis of osteoporosis there has been
a fragility fracture, among which most of the cases affected
the spine. The presence of a vertebral compression frac-
ture increases the risk of further vertebral fractures and it
is associated to an increased mortality among men compared
to women.

Only the 24% of our included patients were diagnosed with
idiopathic osteoporosis, while the rest (69%) had secondary
osteoporosis. Identified causes for secondary osteoporosis
did not differ from those commonly reported in the litera-
ture: steroids, Vitamin D deficiency, chronic renal failure,
hypogonadism, and bone strength, compared to monotherapy with one of
the above mentioned options.

With regards to life style factors of our group relevant for di-
agnosis and treatment of osteoporosis, only about the 50%
was revealed to smoke tobacco or drink alcohol; further-
more only 19.7% declared to eat on a daily basis milk de-
derived products. These three mentioned factors are thought
to be relevant as potential risk factors for the development
of osteoporosis. The NOF guidelines recommend pharma-
cological treatments for individuals with risk factors. The
other risk factors that could prompt pharmacological treat-
ments as per guidelines are: history of vertebral or femoral
fracture, patients with osteoporosis diagnosed following
DEXA Scan (T-score < -2.5 at vertebral or femoral level),
males older than 50 with femoral fracture risk > 3% or frac-
ture risk > 20% according to FRAX (Fracture Risk Assess-
ment Tool).

In our center we treat idiopathic and secondary osteopo-
sis in male patients with zolendronic acid. Other alternative
are denosumab (for idiopathic osteoporosis in males and
iatrogenic osteoporosis following treatment of prostate can-
cer) and stronzium ranelate. Teriparatide is a further option
only for severe cases of idiopathic osteoporosis in males
or in presence of new vertebral or femoral fracture during
treatment with one of the above mentioned options.

Denosumab is a humanised monoclonal antibody that acts
by forming immunocomplex with a binder called RANKL,
which is a protein that works as primary signal in the pro-
motion process of bone remodelling. Teriparatide (hPTH
1-34) is a synthetic recombinant polypeptide (analogue of
the human parathyroid hormone PTH) whose act similar-
ly to PTH by physiologically increasing calcium levels in
the blood by three ways: increasing intestinal absorption
of calcium, renal tubular reabsorption and renal loss of
phosphate. The combined action of these two drugs links to
significant improvement in terms of bone microarchitecture
and bone strength, compared to monotherapy with one of
them (10, 11).

Our study is a descriptive analysis of a selected group
treated at one single specialist center. The size of the group
does not allow us to extend our results to the entire popula-
tion, but they are however based on a significant amount of
cases, all treated at one single center with a standardised
approach.

Bisphosphonates (alendronate, risedronate, zolendron-
ic acid) and teriparatide are the only two pharmaceutical
options with evidence of reducing the risk of fractures in
men. Alendronate and risedronate are able to increase the
bone mass at vertebral and femoral level and to reduce the
risk of vertebral fracture in primary and secondary to ste-
roids osteoporosis in males. Zoledronate has been shown
to improve the bone mass at vertebral and femoral level
and to reduce the risk of re-fracture both in idiopathic osteo-
porosis and secondary to steroids osteoporosis in males.
Denosumab is able to improve the BMD in males at high
risk of fragility fracture and it is recommended in the treat-
ment for reduction of bone mass in individuals on treatment
for prostate cancer with anti-androgens. Stronzium ranel-
ate has revealed to increase bone mass in males treated
against a second group treated with a placebo. Teriparatide
has shown to be able to significantly improve the BMD at
spinal and femoral level and to reduce vertebral fracture
risk. It is also more effective in the treatment of secondary
to steroids osteoporosis compared to alendronate and rise-
dronate, in terms of increasing BMD and reducing the risk
of vertebral fractures (10, 11).

There is still no evidence that any of the mentioned treat-
ment could reduce the risk of compression vertebral frac-
tures in males. The safety of all these medications is similar
to that recorded in the female post-menopause population
with regards to type and number of side effects. In any cas-
es an adequate income of calcium (1000-1200 mg a day)
and Vitamin D (cholecalciferol 800-1000 IU a day) must be
guaranteed despite patients could be on one of the men-
tioned medications. Periodical BMD check in males with a
major risk factor or older than 50 and at least two minor risk
factors or older than 70 even in absence of other risk factor
for fragility fracture are auspicable (10, 11).

With our study we would like to shed the lights on a probably
underestimate issue (osteoporosis in males) and highlight
that the number of male patients with diagnosis of osteo-
porosis is significant, and more studies should by carried
out in order to obtain at least the same level of evidence (in
terms of risk factors and treatments) of those obtained with
regards to female patients.

The results obtained in our study shows how a standardised
approach and more attention for a problem that is routinely
dealt with, but with probably less scientific resources, could
achieve good results in terms of designing a standardised
approach with epidemiology, clinical and radiological as-
pects all involved. On the other hand our data are in keep-
ing with those present in the international literature.

We advocate the need of a high level of evidence study
with bigger group sizes in order to obtain more definitive
guidelines and treatment options in the most possible stan-
dardised way.

Conclusions

The T-score for the diagnostic densitometric cut-off for os-
teoporosis in male patients is < -2.5 DS compared to the
scores applicable for young male individuals. The already
studied pharmacological treatment options should be coa-
diuvated by an adequate intake of calcium and vitamin D.
Alendronate, risedronate, zolendronate, denosumab and
stronzium ranelate are the used medications in our center. Denosomab and stronzium are not recommended for secondary to steroids osteoporosis. In case of severe osteoporosis or in presence of recurrent fragility vertebral or femoral fractures, teriparatide is indicated.

We would like to highlight that osteoporosis in males must be considered as relevant and with same high impact as in females. It is commonly secondary rather than primarily and causes that could bring to diagnosis of osteoporosis should be possibly identified and acted on. In our study more than 50% of the cases was associated to secondary causes, which are preventable or treatable as per definition of “secondary”.

Despite improvements in terms of diagnostic and therapeutic aspects, diagnostic in men is often delayed. It is very important to highlight the importance of early diagnosis of osteoporosis in males within the medical community with the aim to identify those individuals at high risk in order to facilitate early diagnosis and treatment.

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Conflict of interest statement

All Authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

Human and animal right

For this study type is not required any statement relating to studies on humans and animals. All patients gave the informed consent prior being included into the study. All procedures involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

References