Imaging in Osteoporosis: An update.

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Abstract

Osteoporosis is characterised by low bone mineral density and micro-architectural deterioration of bone leading to an increased risk of low trauma fractures, associated morbidity and mortality. This article describes the advances in imaging of osteoporosis including opportunistic identification of low bone density and vertebral fractures. A recap of the imaging required in the diagnosis and management of osteoporosis is also covered since it is important to include imaging within the patient pathway, especially where vertebral fractures are suspected. Additional imaging modalities such as magnetic resonance imaging are important to aid differential diagnosis where the cause of the fracture is unclear. Clinicians reviewing imaging examinations, radiographers and radiologists reporting these must be vigilant for the presence of osteoporosis and play a major role in ensuring these patients have their risks highlighted so that they are put onto the appropriate pathway for diagnosis and treatment. Fracture liaison services provide a robust system for ensuring appropriate capture and follow-up of patients at risk of osteoporosis.

Key words: Osteoporosis, Imaging, Fracture, Diagnosis
Introduction

One in two women and one in five men over the age of 50 will sustain a fracture, most of which are attributable to osteoporosis\(^1\). Osteoporosis is characterised by reduced bone density and micro-architectural deterioration of bone; it is a common metabolic bone disease in the elderly population resulting in an increased risk of fracture\(^2\). Patients with osteoporosis-related fractures describe osteoporosis as a frequently invisible disability which negatively impacts on their life and can have a life changing impact, including the need to cease working or give up enjoyable activities which are not compatible with their risk of fracture\(^3\). Osteoporosis is a major public health issue in the UK, although trends in fracture incidence between 1990 and 2012 demonstrate no significant changes in fracture incidence in those aged 50 and over\(^4\). However, there is an increased incidence of clinical vertebral fractures in women reported over the same period, which may be as a result from improvements in diagnosis and reporting\(^4\). Appropriate diagnosis, therapeutic intervention and monitoring remains a key priority to reduce the burden of osteoporosis-related fractures. This paper will discuss the use of imaging in the opportunistic diagnosis, differential diagnosis and monitoring of osteoporosis.

Patients presenting with fragility fractures

Osteoporosis can lead to fractures anywhere in the skeletal system, although fractures of the wrist, hip and vertebrae are the most commonly seen.\(^5\) Patients presenting with low trauma fragility fractures or those who have notable x-ray osteopenia should be referred for a DXA scan\(^6\). Figures 1a and 1b demonstrate a Colles’ fracture with marked x-ray osteopenia. X-ray osteopenia can be identified by reduced cortical thickness with an associated appearance of reduced density and more prominent trabeculation being visualised on a radiograph, frequently providing less contrast between the bone and soft tissues than when compared to radiographs of normal density bone\(^7\). Whilst osteoporosis may be suspected from these radiographic findings, this is not a reliable way of making the diagnosis and projection radiography is not indicated for the assessment of osteoporosis in the absence of the requirement for fracture diagnosis. Projection radiography remains the first line imaging choice in many incidents where there is clinical suspicion of a fracture such as vertebral or appendicular fracture. However, in the case of a cervical spine fracture, computed tomography (CT) is recommended in the first instance due to the difficulties of interpretation of radiographs in the elderly population\(^8\). Some patients who have clinical signs and
symptoms of a fracture, but without radiographic confirmation may have and occult fracture. These are of particular importance in the hip, where identifying the fracture quickly to ensure the patient reaches theatre with twenty-four hours is of utmost importance\textsuperscript{9}. In this case the ideal pathway providing the greatest diagnostic accuracy is to perform an magnetic resonance imaging (MRI) scan (figure 2), where the bone marrow oedema associated with the occult fracture can confirm its presence\textsuperscript{10}. In patients who are not suitable for MRI, or where MRI is not available, CT can be used as an alternative, though has a marginally poorer accuracy\textsuperscript{10,11}. Post imaging, the most effective way of ensuring patients presenting with a fracture are referred for a DXA and have appropriate assessment for osteoporosis is via a fracture liaison service\textsuperscript{12}.

**Diagnosis**

Dual energy x-ray absorptiometry (DXA) remains the most widely accepted method for the assessment of osteoporosis\textsuperscript{13}. While the UK currently does not have a screening programme for osteoporosis\textsuperscript{14}, the SCOOP study has demonstrated that screening is a cost effective tool for preventing fractures in older women aged between 70 and 85 years using a combination of FRAX and bone mineral density (BMD) measurements\textsuperscript{15}. Identification of patients who need bone assessment can be aided by tools such as FRAX and QFRACTURE which also independently predict fracture risk using modelling based on clinical risk factors\textsuperscript{16, 17, 18}. Early diagnosis allows treatment for osteoporosis before a fragility fracture has occurred and NICE recommends considering assessing the risk of fragility fracture in all women aged 65 years and over and all men aged 75 years and over as well as patient with clinical risk factors over 50 years with and in those younger than 50 years with major risk factors\textsuperscript{19}. Falls history should also be considered alongside bone mineral density and clinical risk factors when deciding on therapeutic intervention, since it provides a further independent risk factor for fracture\textsuperscript{20}.

**Vertebral fracture assessment**

Dual x-ray absorptiometry scanners can also be utilised for vertebral fracture assessment (VFA), as demonstrated in figure 3. VFA provides a lateral image of T4 to L4, and has a significantly reduced dose compared to a thoraco-lumbar projection radiography series\textsuperscript{21}. It has been reported to have a high degree of accuracy for diagnosing fracture and in practice can increase the identification of vertebral fractures and altered patient management in
those with unknown fractures. The presence of a vertebral fracture can lead to pain, deformity and loss of function, but importantly is also a strong predictor of future fracture. Vertebral fracture diagnosis remains suboptimal and many sufferers have multiple fractures prior to diagnosis. Using VFA in practice has been demonstrated to increase the number of patients diagnosed with osteoporosis and requiring therapeutic intervention.

If a vertebral fracture is identified on a VFA scan, then radiographs are required to differentiate between non-fracture deformities such as Scheuermann’s disease or degenerative changes, or to examine for another pathology causing the fracture, for example Paget’s disease of bone or malignancy. Further imaging may be required where other underlying pathology is suspected and MRI, CT, Nuclear Medicine or PET-CT may be used depending on the pathology suspected. MRI and PET-CT in combination have been demonstrated to have high sensitivity and specificity for benign and malignant lesions in the spine, with 100% accuracy in the former. Figures 4a and 4b demonstrate a vertebral fracture resulting from metastatic disease.

Vertebral fractures where the patient continues to have pain despite optimal pain management, should be investigated using clinical examination and or imaging to confirm the pain is at the site of the fracture. Magnetic resonance imaging can be particularly useful if considering a vertebroplasty or kyphoplasty. However, a recent Cochrane review reported moderate to high quality evidence that vertebroplasty has little benefit for treating acute or subacute vertebral fractures in routine clinical practice when compared to a sham procedure. Patients with osteoporosis suffering from low back and pelvis pain should have sacral insufficiency or stress fractures considered as part of their differential diagnosis. These occasionally also occur in the final trimester of pregnancy and postpartum in younger women. Computed tomography or MRI provide better sensitivity and specificity, with MRI being considered the current gold standard for sacral insufficiency fractures.

**Differential diagnosis**

The presence of apparent osteoporosis on a DXA measurement, with or without fracture, may not provide the definitive diagnosis. Vitamin D deficiency is becoming increasingly prevalent among the elderly population within the UK and therefore osteomalacia should be ruled out by blood tests, particularly in those who are immobile and do not go outside often. There are occasionally some findings in osteomalacia which are not seen in osteoporosis. A “Looser’s zone” or pseudofracture, may be seen in osteomalacia along with reports of bone pain and muscle weakness, which are not typical symptoms of osteoporosis.
Multiple myeloma can cause lytic lesions, which improve with chemotherapy but the x-ray appearance may also be one of diffuse osteopenia, mimicking osteoporosis. There should be a low index of suspicion for this condition and patients with suspected Multiple Myeloma may be screened by blood tests looking for anaemia, abnormal protein levels and raised plasma viscosity and further assessment of urine for Bence Jones protein and plasma electrophoresis where diagnosis is strongly suspected. Finally, occasional anatomical anomalies are visualised on DXA scans which may or may not impact on the BMD results. If these are unexplained, then further imaging may be required to investigate these.

Opportunistic identification of low bone mineral density and vertebral fractures

Around 30% of vertebral fractures are asymptomatic and do not come to clinical attention or are undiagnosed at the point patients present with pain. This has resulted in an interest in opportunistic identification of vertebral fractures from imaging undertaken for other clinical reasons. This includes CT, MRI and radionuclide or PET scans as well and projection radiographs. Multi-planar sagittal reconstructions (Figure 5) of CT scans enable easier visualisation of vertebral fractures than the traditional axial slices and education for all clinicians to look for and report vertebral fractures is a key requirement for improving outcomes in patients with osteoporosis and vertebral fractures.

Further opportunistic identification of low bone mineral density comes from CT scans using asynchronous techniques. Traditionally, CT measurements of BMD have required the patient to be scanned with a phantom within the field of view. However, asynchronous BMD measurement using CT means that a phantom can be scanned weekly and the Hounsfield numbers of bone compared to the phantom, yielding a bone mineral density measurement for patients who are having CT scans for potentially unrelated reasons. This technology is still developing an evidence-base and it is not currently used in general clinical practice, however, it affords opportunities for the future to improve the identification of those at risk of fragility fractures.

Emerging computer aided detection technologies aiming to better identify and classify incidental vertebral fractures from CT and projection radiography, as well as estimating osteoporotic risk based on cortical thickness of commonly performed imaging such as orthopantomography (OPG) are developing. Although these currently remain predominately
in the research phase, they may potentially help in the future to address the high miss rate of these clinically important findings that are predictive of future osteoporotic fracture 33 34.

Longitudinal monitoring

A diagnosis of osteoporosis requires the consideration of therapeutic intervention in line with national and local guidelines and in line with clinical decision making in relation to the clinical history of the patient42 43. The monitoring of treatment responses in patients can assist with adherence and compliance, which is currently poor for those taking bisphosphonates44,45. However, the use of DXA in treatment monitoring is often sub-optimal, with time intervals between 18 to 24 months to reliably measure changes as a result of therapeutic interventions 46. Biochemical markers of bone turnover are an appropriate alternative where available and can detect treatment response much more rapidly than DXA, with a reliable result just three months post commencing treatment47. Monitoring of BMD five to ten years post commencing treatment is of particular use when considering a drug treatment holiday for patients on bisphosphonates to prevent the over suppression of bone turnover. Further monitoring may be required during the treatment holiday when an increase in bone turnover markers and a reduction in BMD may signal the requirement to recommence treatment48.

Bisphosphonates have been demonstrated to be effective at increasing BMD and reducing fractures by approximately 50% over 2 years of use49. However, as the longevity of bisphosphonates has increased, adverse events in long-term users, generally of greater than five years have been reported. Atypical fractures of the femora (figure 6) in men and women have been reported in a number of studies. These fractures share a common appearance, with periosteal thickening as often seen in stress fractures. The fractures also tend to be transverse and in the upper third of the femur50 51. Projection radiography is the most common method for diagnosing these fractures and additional imaging is rarely required; the important thing is for radiologists and physicians to be aware of the imaging findings and to suspect the condition when patients on bisphosphonate therapy present with new hip, groin or thigh pain. Bilateral atypical femoral fractures also occur in a proportion of cases and a low threshold for imaging the contra-lateral femur in cases of incomplete or complete atypical femoral fracture is recommended 52,53 54. If there is doubt on radiographic images MRI or radionuclide imaging may be helpful.
Osteonecrosis of the jaw (ONJ) is a rare, but notable complication of those on long term and especially high dose bisphosphonates, such as those with metastatic bone disease\textsuperscript{55}. Imaging for this is required to ascertain the extent and differentiate from metastatic disease. Nuclear medicine scintigraphy provides the ability for early diagnosis and other imaging may include dental radiographs, orthopantomographs (OPG’s), MRI and CT to investigate the extent and assist in differential diagnosis of ONJ\textsuperscript{56}.

\textit{Conclusion}

In conclusion, imaging plays an integral role in the diagnosis and management of osteoporosis, osteoporotic fractures and the complications associated with bisphosphonate treatment. Opportunistic identification of vertebral fractures and low bone mineral density is increasing and these are likely to become standard practice in the future. Additional imaging modalities such as MRI can aid differential diagnosis where the cause of the fracture is unclear and it is important to include imaging within the patient pathway where vertebral fractures are suspected. Radiographers and radiologists reporting imaging examinations have a duty to identify and report vertebral fractures as such and highlight the need for osteoporosis assessment. Fracture liaison services provide an evidence-based provision to ensure that patients presenting with fractures are directed into osteoporosis services.
References

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Figure 1a Postero-anterior wrist radiograph demonstrating a Colles' fracture and x-ray osteopenia
Figure 1b Lateral wrist radiograph demonstrating a Colles’ fracture and x-ray osteopenia
Figure 2: MRI showing occult femoral neck fracture
Figure 3: GE Lunar Prodigy dual energy lateral vertebral assessment scan, utilising morphometric software to indicate fracture presence and grade.
Figure 4a: MRI of vertebral fracture from metastasis
Figure 4b: MRI of vertebral fracture from metastasis
Figure 5 Sagittal multi-planar reconstruction of a CT scan demonstrating an incidental finding of osteoporosis related vertebral fractures at T6 and T8.
Figure 6: Radiograph of an atypical femoral fracture