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Abstract

Rheumatoid arthritis (RA), an autoimmune disease, is characterized by the presence of symmetric polyarthritis predominantly of the small joints that leads to severe cartilage and bone destruction. Based on animal and human data, the pathophysiology of osteoporosis, a frequent comorbidity in conjunction with RA, was delineated. Autoimmune inflammatory processes, which lead to a systemic upregulation of inflammatory and osteoclastogenic cytokines, the production of autoantibodies, and Th cell senescence with a presumed disability to control the systemic immune system's and osteoclastogenic status, may play important roles in the pathophysiology of osteoporosis in RA. Consequently, osteoclast activity increases, osteoblast function decreases and bone metabolic and mechanical properties deteriorate. Although a number of disease-modifying drugs to treat joint inflammation are available, data on the ability of these drugs to prevent fragility fractures are limited. Thus, specific treatment of osteoporosis should be considered in patients with RA and an associated increased risk of fragility fractures.

Aim:

This study aims to show the effect of disease activity of rheumatoid arthritis on possibility of osteoporosis.

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Liqaa shihab

Content

Introduction

Rheumatoid arthritis

It is a chronic autoimmune disease that primarily affects the joints, causing inflammation and damage. It is estimated that approximately 1% of the world's population has rheumatoid arthritis, and women are more likely to be affected than men.

Causes:

The exact cause of rheumatoid arthritis is not fully understood, but it is believed to be caused by a combination of genetic and environmental factors. Certain genes are known to increase the risk of developing rheumatoid arthritis.

Symptoms:

The symptoms of rheumatoid arthritis can vary from person to person, but the most common symptoms include:

● Joint pain, swelling, and stiffness: These symptoms typically affect the smaller joints in the hands and feet, but can also occur in larger joints such as the knees and shoulders.

● Fatigue: Many people with rheumatoid oid arthritis experience fatigue, which can be severe and debilitating.

● Morning stiffness: Stiffness in the joints, particularly in the morning, is a common symptom of rheumatoid arthritis.

● Reduced mobility: Over time, rheumatoid arthritis can cause joint damage and deformity, which can reduce mobility and make it difficult to perform daily activities.

Diagnosis

involves a combination of clinical evaluation, laboratory tests, and imaging studies. The diagnosis process typically involves the following steps:

● Medical history and physical exam

● Blood tests: Blood tests can help to detect the presence of specific antibodies that are associated with RA, such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies. Elevated levels of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may also indicate the presence of inflammation.

● Imaging studies: X-rays, ultrasound, and MRI scans can be used to assess joint damage and inflammation. These imaging studies can also help to rule out other conditions that may cause joint pain and swelling.

● Diagnosis criteria: The American College of Rheumatology (ACR) has established diagnostic criteria for RA based on clinical symptoms and laboratory findings. These criteria include the presence of joint pain, swelling, and stiffness lasting for more than six weeks, as well as the presence of specific antibodies and elevated levels of inflammatory markers.

Treatment:

The goals of treatment for rheumatoid arthritis are to reduce inflammation, relieve pain, and improve joint function.

The following are some common treatments for rheumatoid arthritis:

● Nonsteroidal anti-inflammatory drugs (NSAIDs)

● Disease-modifying antirheumatic drugs (DMARDs): DMARDs can help to slow down the progression of rheumatoid arthritis and prevent joint damage. Examples of DMARDs include methotrexate, sulfasalazine, and hydroxychloroquine.

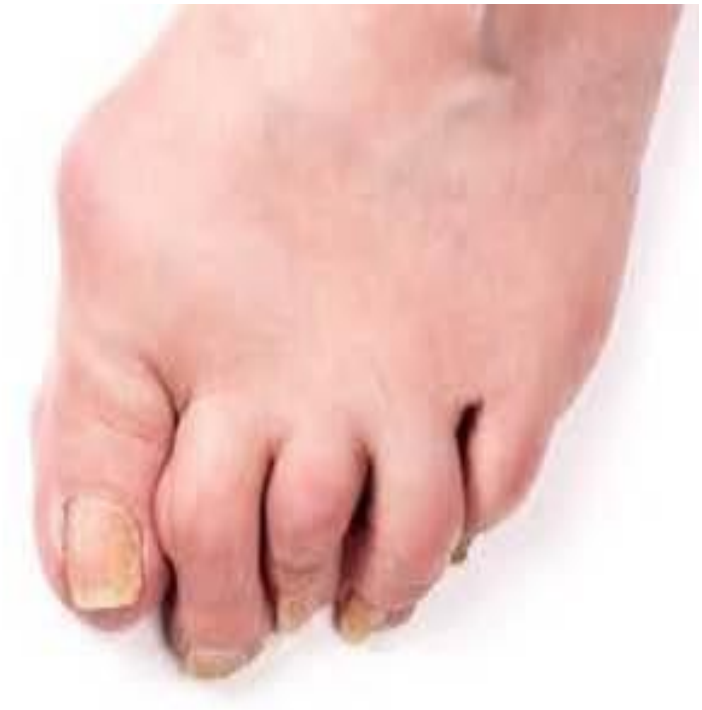
● Biologic drugs: Biologic drugs target specific proteins in the immune system, Examples include etanercept, adalimumab, and infliximab.

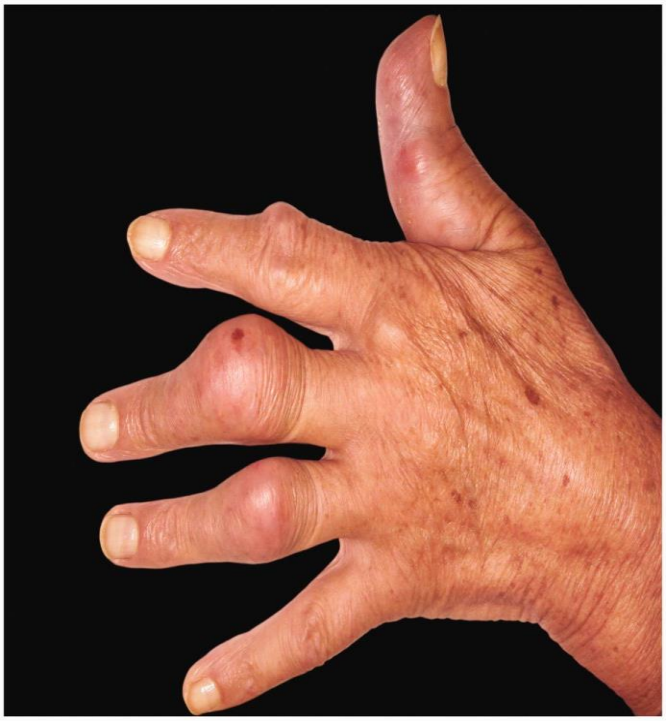
● Corticosteroids: Corticosteroids can help to reduce inflammation and relieve pain, but they are typically used for short-term treatment due to the risk of side effects.

● In addition to medication, physical therapy and exercise can also be beneficial

Osteoporosis and rheumatoid arthritis are two conditions that can affect the musculoskeletal system, leading to significant health implications. Osteoporosis is a condition characterized by the loss of bone mass and density, leading to an increased risk of fractures. Rheumatoid arthritis, on the other hand, is an autoimmune disorder that causes inflammation and damage to the joints, leading to pain and stiffness.

While these conditions are distinct, there is growing scientific interest in the potential relationship between them. Several studies have suggested that there may be a link between osteoporosis and rheumatoid arthritis, and further research is needed to better understand this relationship.





Osteoporosis

It is a Disease in which low bone mass and micro-structural deterioration of bone tissue lead to increased bone fragility, is the most common metabolic bone disease in the United States. it is often overlooked and undertreated, in large part because it is clinically silent; there are no symptoms before a fracture occurs

Signs and symptoms

Osteoporosis may does not become clinically apparent until a fracture occurs and so is sometimes referred to as the “silent disease.” Two-thirds of vertebral fractures are painless,

Typical findings in patients with painful vertebral fractures may include the following:

◇ The episode of acute pain may follow a fall or minor trauma.

◇ Pain is localized to a specific, identifiable, vertebral level

◇ paravertebral muscle spasms exacerbated by activity and decreased by lying supine.

On physical examination we will found ||

○ point tenderness over the involved vertebra

○ Thoracic kyphosis with an exaggerated cervical lordosis (dowager's hump) ○ loss of lumbar lordosis

Diagnosis

Baseline laboratory studies include the following:

□ Complete blood count

□ Liver function tests

□ Thyroid-stimulating hormone level

□ 25-Hydroxyvitamin D level

□ Serum protein electrophoresis

□ 24-hour urine calcium/creatinine

□ Testosterone, LH and FSH serum level

Dual-energy x-ray absorptiometry (DXA) is currently the criterion standard for the evaluation of Bone mineral density (BMD)

Vertebral imaging is also recommended for postmenopausal women and men age 50 and older

plain radiography features and recommendations are as follows:

- Obtain radiographs of the affected area in symptomatic patients.

- Lateral spine radiography can be performed

- Radiographic findings can suggest the presence of osteopenia or bone loss but cannot be used to diagnose osteoporosis.

- Radiographs may also show other conditions, such as osteoarthritis, disk disease, or spondylolisthesis.

Management :

Lifestyle modification /

● Increasing weight-bearing and muscle-strengthening exercise

● Ensuring optimum calcium and vitamin D intake and balanced diet

● Tobacco cessation

● Limiting alcohol consumption

● Removing potential risk factors to avoid falls

Pharmacologic therapy /

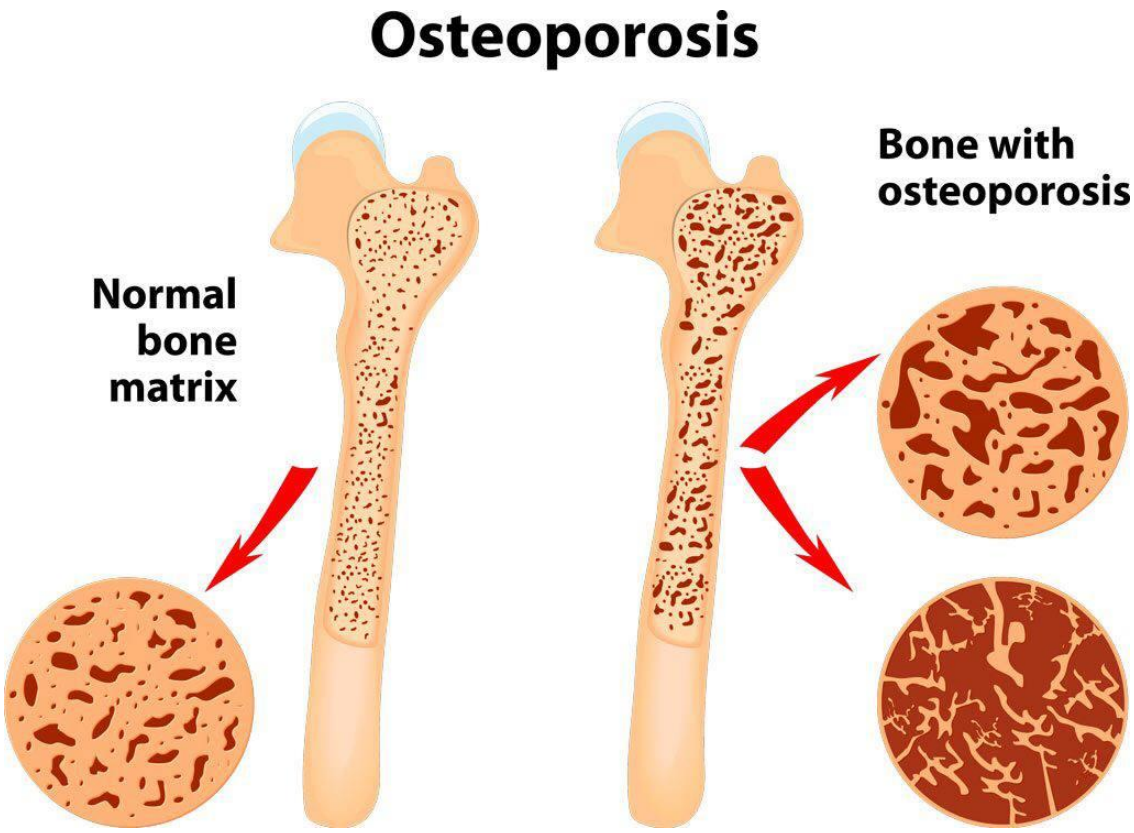
● Bisphosphonates: Bisphosphonates are the most commonly prescribed drugs for osteoporosis. Some examples of bisphosphonates include alendronate, risedronate, and ibandronate.

●Selective estrogen receptor modulators (SERMs): SERMs are drugs that mimic the effects of estrogen on bone tissue. They can help to prevent bone loss, Raloxifene is an example of a SERM.

● Teriparatide: it is a form of parathyroid hormone that stimulates the growth of new bone tissue.

● Denosumab: it is a monoclonal antibody that inhibits a protein called RANKL, which plays a role in bone resorption.

● Calcitonin: Calcitonin is a hormone that helps to regulate calcium levels in the body. It can also inhibit bone resorption and reduce the risk of fractures. Calcitonin is typically used as a second-line treatment for osteoporosis



Result:

IN Related to age

in patient with osteopenia (10)

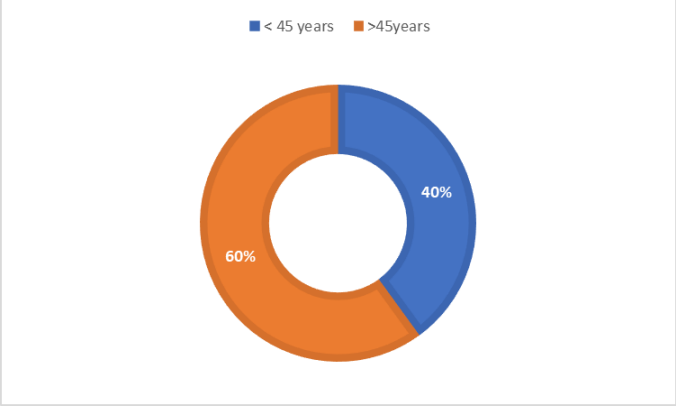
4 patient 40% less than 45 years old

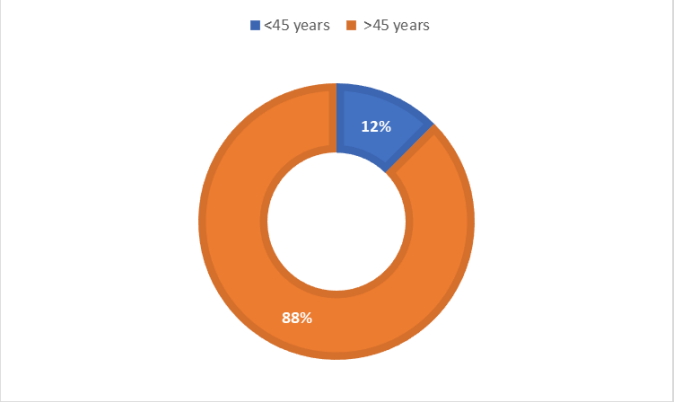
6 patient 60% more than 45 years old

WHILE in osteoporosis (8)

7paient about 87.5% were >45 years old

and one patient 12.5% WAS <45 years old





IN Related to gender all patient with osteoporosis were female 100%

May be that because the hormone changes that happen at the menopause directly affect bone density. The female hormone oestrogen is essential for healthy bones. After the menopause, oestrogen levels fall. This can lead to a rapid decrease in bone density

In related to disease duration

Patient with osteopenia

50% of them were with disease duration >5 years old while in patient with osteoporosis all of them 100% were with disease duration >5 years.

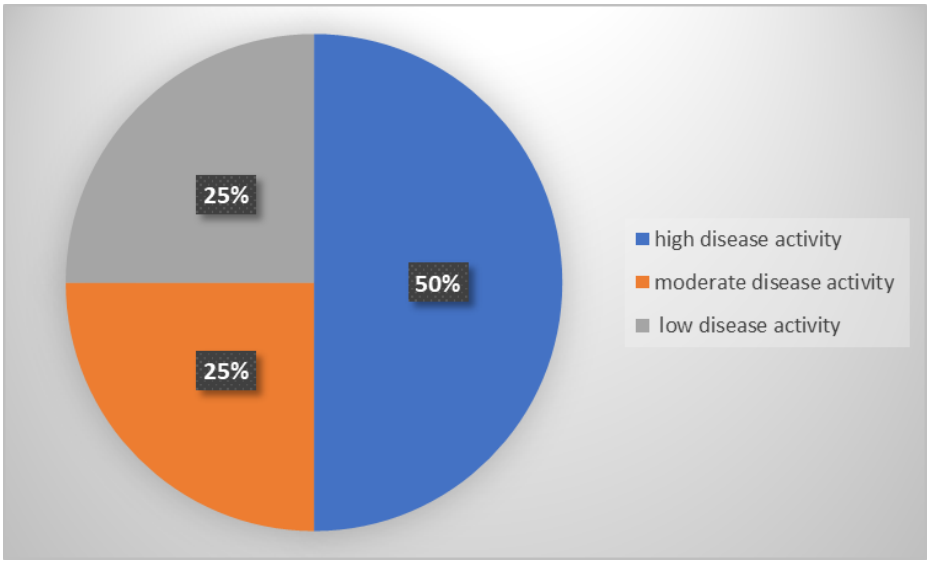
IN Related to disease activity

Patient with osteoporosis

4(50%) high disease activity

2 (25٪) modrate disease activity

2 (25%) low disease activity



Conclusion:

As we note the highest prevalence of osteoporosis among patients with rheumatoid arthritis was seen significantly among older patients ,female patient, patients with a longer duration of rheumatoid arthritis and those with high activity of rheumatoid arthritis

Method:

in this cross-sectional study we took 20 patient with rheumatoid arthritis

we collected the following parameters

1- AGE

2-GENDER

3-DISEASE DURATION

4-DISASE ACTIVITY BY USING CLINICAL DISEASE ACTIVITY INDEX (CDAI)

which divided disease activity into four categories

>22 is high disease activity

10-22 moderate high disease

3-10 low high disease

5- TREATMENT

6-SMOKING

7-BODY MAX INDEX

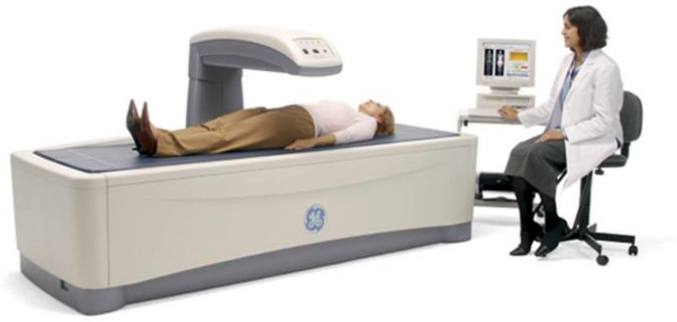
WE sent those patient for dual energy X ray absorption DEXA SCAN

the result of the scan were categorized into three category :

1) osteoporosis > -2.5

2)osteopenia (-1)-(-2.5)

3) normal < -1



Discussion

This study revealed that 40% of patients with rheumatoid arthritis had osteoporosis. This agrees with the results of Lee et al [9] which showed that about 50 % of patients with RA in their study had osteoporosis. also agrees with the results of Hauser et al [10] which showed that up to 50 % of

postmenopausal females with RA had osteoporosis. The results was disagreed with the the results of Miculs et al [11] which showed that the prevalence of osteoporosis in RA patients was 10 %. This difference may be due to those patients included in their study was only those with disease duration less than two years which may affect the possibility of osteoporosis occurrence, while in our study there was no restriction regarding disease duration.

The results of this study concluded that the highest prevalence of osteoporosis was among those with older age, longer disease duration, higher disease activity, and in patients with a history of irregular usage of treatment which occur either due to patient incompliance or due to delayed diagnosis.

This agrees with the results of Van Staa et al [12] which showed that osteoporosis is more prevalent in RA patients with long- standing disease due to the effects of chronic systemic inflammation. It also agreed with the results of Lee et al [9] which mentioned that osteoporosis in RA is more prevalent among older patients due to the effect of age which is a known risk factor for osteoporosis. It also agrees with the results of Phuan-Udom et al [6] which showed that osteoporosis was more prevalent in RA patients who have higher disease activity.

During our practice, we face a number of cases that do not take effective RA treatment regularly. This occurs either due to patient incompliance or due to delay in diagnosis of the patient. This leads to less control of the systemic effect of the disease and more damage to the bone by this chronic systemic inflammation.

In this study, among those patients with osteoporosis, 41.7 % were sub-grouped as having severe osteoporosis which is defined as osteoporosis plus at least one fragility fracture.As mentioned in the Table (3), 52.6% of those who received treatment irregularly had severe osteoporosis with a significant association between the treatment regularity of rheumatoid arthritis and severe

osteoporosis. This indicates that the most important predictive measure for osteoporosis severity in RA patients is the regularity of treatment.

Recommendation:

The patient should be diagnosed early and probably to prevent OSTEOPOROSIS

And give the patient some advice

- try to eat optimal nutrition in the youth to achieve high peak bone mass, including adequate intake of calcium and vitamin D.
- Do regular weight-bearing exercise.
- Identification and treatment of subjects with vitamin D deficiency, especially in children, females in the reproductive age group, and the elderly.
- Avoidance of tobacco smoking and alcohol intake.
- Assessment of every postmenopausal woman for risk of osteoporosis to determine the need for diagnostic tests and prevention /treatment.
- Early treatment of secondary causes of osteoporosis [for example, thyrotoxicosis, smoking, primary hyperparathyroidism, others].
- Prevention and early treatment of osteoporosis of patients who are receiving high-dose steroid therapy, or other drugs that may contribute to osteoporosis

Reference :

1. National Institutes of Health Osteoporosis and Related Bone Diseases National Resource Center 800-624-2663 202-466-4315 (TTY) NIHBoneInfo@mail.nih.gov(link sends email)

www.bones.nih.gov (http://www.bones.nih.gov/)

2.Rheumatoid arthritis. National Institute of Arthritis and Musculoskeletal and Skin Diseases. https://www.niams.nih.gov/Health_Info/Rheumatic_Disease/default.asp. Accessed Feb. 9, 2021.

3. Rheumatoid arthritis. American College of Rheumatology. https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Rheumatoid-Arthritis. Accessed Feb. 9, 2021.

4.Matteson EL, et al. Overview of the systemic and nonarticular manifestations of rheumatoid arthritis. https://www.uptodate.com/contents/search. Accessed Feb. 9, 2021.

5. Goldman L, et al., eds. Rheumatoid arthritis. In: Goldman-Cecil Medicine. 26th ed. Elsevier; 2020. https://www.clinicalkey.com. Accessed Feb. 9, 2021.

6. Ferri FF. Rheumatoid arthritis. In: Ferri's Clinical Advisor 2021. Elsevier; 2021. https://www.clinicalkey.com. Accessed Feb. 9, 2021.

7. Kellerman RD, et al. Rheumatoid arthritis. In: Conn's Current Therapy 2021. Elsevier; 2021. https://www.clinicalkey.com. Accessed Feb. 9, 2021.

8. Moreland LW, et al. General principles and overview of management of rheumatoid arthritis in adults. https://www.uptodate.com/contents/search. Accessed Feb. 9, 2021.

9. Xeljanz, Xeljanz XR (tofacitinib): Drug safety communication — Initial safety trial results find increased risk of serious heart-related problems and cancer with arthritis and ulcerative colitis medicine. https://www.fda.gov/safety/medical-product-safety-information/xeljanz-xeljanz-xr-tofacitinib-drug-safety-communication-initial-safety-trial-results-find-increased. Accessed Feb. 23, 2021.

10. Office of Patient Education. Arthritis: Caring for your joints. Mayo Clinic. 2017.

11. Living with arthritis. American Occupational Therapy Association. https://www.aota.org/About-Occupational-Therapy/Patients-Clients/Adults/Arthritis.aspx. Accessed Feb. 23, 2021.

12.Renaldi RZ. Total joint replacement for severe rheumatoid arthritis. https://www.uptodate.com/contents/search. Accessed Feb. 9, 2021.

13. Rheumatoid arthritis: In depth. National Center for Complementary and Integrative Health. https://www.nccih.nih.gov/health/rheumatoid-arthritis-in-depth. Accessed Feb. 23, 2021.

14. Chang-Miller A (expert opinion). Mayo Clinic. Feb. 27, 2021. National Institute of Arthritis and Musculoskeletal and Skin Diseases (https://www.niams.nih.gov/Health_Info/Rheumatic_Disease/default.asp)

15. Ruddy S, Harris ED, Jr, Sledge CB, Budd RC, Sergent JS. (eds). Kelley's Textbook of Rheumatology, 7th edn. Philadelphia: Elsevier, 2005. [Google Scholar]

(https://scholar.google.com/scholar_lookup?title=Kelley%27s+Textbook+of+Rheumatology&publication_year=2005&)

16. Stanmore E, Oldham J, Skelton D, et al. Fall incidence and outcomes of falls in a prospective study of adults with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2013;65:737–44. [PMC free article] (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4471630/?report=reader) [PubMed] (https://pubmed.ncbi.nlm.nih.gov/23139011) [Google Scholar] (https://scholar.google.com/scholar_lookup?journal=Arthritis+Care+Res+(Hoboken)&title=Fall+incidence+and+outcomes+of+falls+in+a+prospective+study+of+adults+with+rheumatoid+arthritis&author=E+Stanmore&author=J+Oldham&author=D+Skelton&volume=65&publication_year=2013&pages=737-44&pmid=23139011&)

17. Shimizu T, Takahata M, Kimura-Suda H, et al. Autoimmune arthritis deteriorates bone quantity and quality of periarticular bone in a mouse model of rheumatoid arthritis. Osteoporos Int 2016;28:709–18. [PubMed] (https://pubmed.ncbi.nlm.nih.gov/27704183) [Google Scholar] (https://scholar.google.com/scholar_lookup?journal=Osteoporos+Int&title=Autoimmune+arthritis+deteriorates+bone+quantity+and+quality+of+periarticular+bone+in+a+mouse+model+of+rheumatoid+arthritis&author=T+Shimizu&author=M+Takahata&author=H+Kimura-Suda&volume=28&publication_year=2016&pages=709-18&pmid=27704183&)