
بسم الله الرحمن الرحیم

Glucocorticoid Induced Osteoporosis

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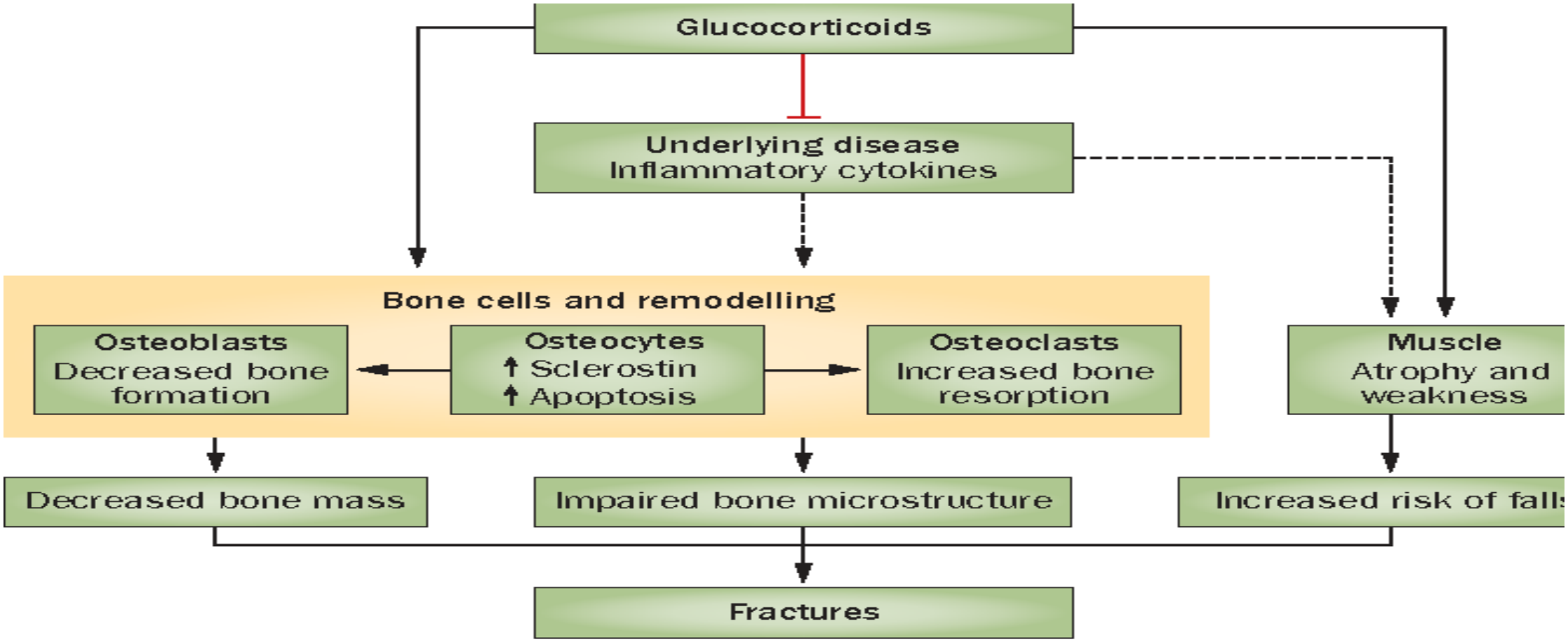
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Introduction

- Up to 25% of patients taking systemic glucocorticoid therapy will develop fractures.
- Under-treatment of GIOP is widely recognized.
- GIOP is the most common cause of secondary osteoporosis.
- Continuous oral glucocorticoid therapy is associated with rapid bone loss and an increase in fracture risk within 3–6 months of initiation and is dose-related.

Physiopathology of GIOP in inflammatory diseases



Rizzoli, R. & Biver, E. Nat. Rev. Rheumatol. advance online publication 11 November 2014

Fracture in GIOP

- Fracture occurs at a higher BMD in individuals receiving GC than in non-glucocorticoid treated people.

- This independent effect on fracture risk may be due to several factors, including:
  - Increased falls risk.
  - Alterations in bone quality that are not captured by BMD.

Glucocorticoid-induced osteoporosis: an update. Endocrine 2018.61(7-16)

Changes in BMD and bone microarchitecture

GC have adverse effects on spine bone microarchitecture detected by HRpQCT and TBS that are independent of BMD and which may contribute to increased fracture risk.

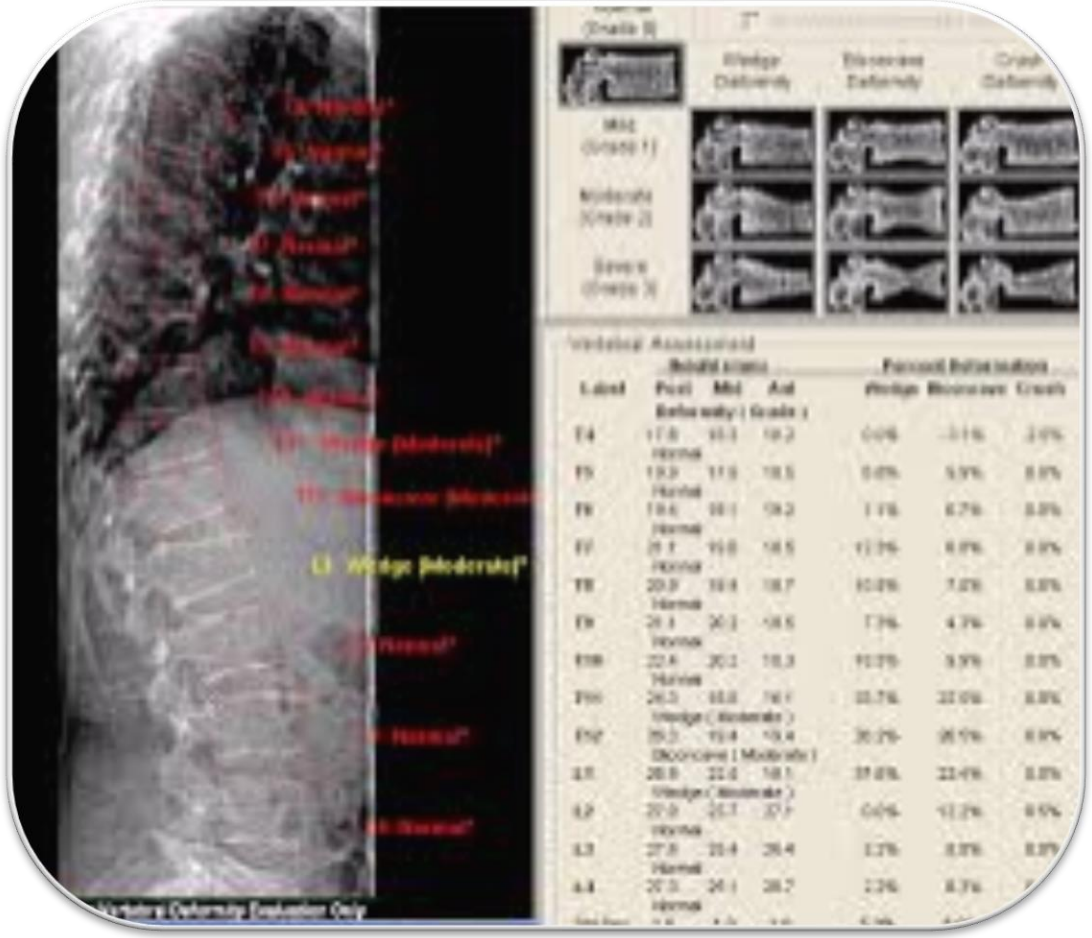
The impact of glucocorticoid therapy on trabecular bone score in older women. *Osteoporos. Int* 2015;26:1773–80.

The interval of serial bone density testing remains controversial

- There are no clear data on frequency of BMD screening.
- Factors that will influence the frequency of testing include :
  - The presence of additional risk factors for fracture
  - The results of the previous BMD
  - The dose of steroids
  - And the rate of change of the BMD
- Patients recently starting GC or those with multiple other risk factors or a history of fracture may need BMD measurement every 6 months, while those with more stability may have BMD measured , once every 3 years.

Vertebral fracture assessment





Considered in all postmenopausal women and men age >50 years if there is a history of, recent or current long-term oral glucocorticoid therapy for screening of fracture. (NOF 2014)

Guidelines for the management of GIOP

ARTHRITIS & RHEUMATOLOGY
Vol. 69, No. 8, August 2017, pp 1521–1537
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SPECIAL ARTICLE

2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

Lenore Buckley,[1] Gordon Guyatt,[2] Howard A. Fink,[3] Michael Cannon,[4] Jennifer Grossman,[5] Karen E. Hansen,[6] Mary Beth Humphrey,[7] Nancy E. Lane,[8] Marina Magrey,[9] Marc Miller,[10] Lake Morrison,[11] Madhumathi Rao,[12] Angela Byun Robinson,[13] Sumona Saha,[6] Susan Wolver,[14] Raveendhara R. Bannuru,[12] Elizaveta Vaysbrot,[12] Mikala Osani,[12] Marat Turgunbaev,[15] Amy S. Miller,[15] and Timothy McAlindon[12]

Buckley L, et al. *Arthritis & Rheumatology* 2017;69(8):1521-37.

Management of GIOP
General measures

- Falls risk should be assessed and preventive measures instituted.
- Exercise, tailored to the individual patient.
- Good nutrition with adequate dietary calcium intake .
- Avoidance of smoking, alcohol abuse.
- Maintenance of an adequate vitamin D status.
- Keeping the dose of glucocorticoids to minimum, with the use of steroid-sparing drugs such as methotrexate or azathioprine .
- ACR 2017 recommend using FRAX algorithm for decision making in GIOP.

FRAX limitations in GIOP

FRAX will underestimate the probability of fracture in GIOP

BMD used in the FRAX tool is the femoral neck, while GIO more heavily affects sites with more trabecular bone such as the lumbar spine, so FRAX will underestimate the probability of fracture.

FRAX cannot be used in people less than 40 years of age

All patients on chronic glucocorticoids over the age of 40 should have BMD and FRAX calculation within 6 months of initiation of glucocorticoids.

GC therapy is in FRAX as dichotomous variable.

“Yes” is entered if there is current exposure to oral glucocorticoids or past exposure for ≥ 3 months at a dose of 5 mg/day or more of prednisolone .

Fracture risk categories in GC-treated patients ≥ 40 years of age

High fracture risk	Moderate fracture risk	Low fracture risk
• Prior osteoporotic fracture • Hip or spine osteoporosis in men age >50 years and postmenopausal women • FRAX MOF (GC-adjusted) >20% FRAX (GC-adjusted) of hip fracture >3%	• FRAX (GC-adjusted) 10-year risk of 10>MOF<19% • FRAX (GC-adjusted) 10-year risk of 1%> HF <3%	• FRAX (GC-adjusted) MOF<10% FRAX • FRAX (GC-adjusted) 10-year risk of hip fracture <1%

Fracture risk categories in GC-treated patients < 40 years of age

High fracture risk	Moderate fracture risk	Low fracture risk
• Prior osteoporotic fracture	• Hip or spine BMD, Z score < - 3 • Rapid bone loss (> 10 % at the hip or spine over 1 year) and • Continuing GC treatment at >7.5 mg/day for > 6 months.	• None of above risk factors

ACR 2017 guidelines recommend pharmacologic intervention in adults

With:

- Moderate or high risk for fracture
- Those treated with very high dose of glucocorticoids(>30 mg /d).

ACR 2017 treatment guide

- Oral bisphosphonates as the first line of treatment in all GIOP patients not of childbearing potential .
- Zoledronic acid, teriparatide, denosumab, and raloxifene as the second, third, fourth, and fifth lines of treatment, respectively, for patients who do not tolerate oral bisphosphonates.



Bisphosphonate in premenopausal woman

- Bisphosphonates are retained in bones for extended duration and are able to cross the placenta.
- Clinicians must exercise caution in prescribing bisphosphonates in pre-menopausal women.
- Based on bone turnover marker studies, some authors recommended a washout period of 5 years for alendronate and zoledronate, and 2 years for risedronate before conception.

Sokal A, et al. Bisphosphonates during pregnancy: a prospective study. Ann Rheum Dis 2016; 75: 93.

Other International guidelines on GIOP treatment

- Numerous groups have developed societal and national guidelines for GIOP.
- Some differences and similarities exist between the more recent national and international guideline on the treatment of GIOP .

NOGG 2017:

Clinical guideline for the prevention and treatment of osteoporosis

The UK National Osteoporosis Guideline Group (NOGG) suggests therapies for:

- Women and men age ≥ 70 years, with a previous fragility fracture, or who are taking high doses of glucocorticoids (≥ 7.5 mg/day prednisone).
- They recommend that in all other individuals, the risk should be assessed with FRAX.

ClinicalEdge™ Summaries of Must-Read Clinical Literature, Guidelines, and FDA Actions

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FDA Approves Prolia for GIOP in Men and Women

FirstWord Pharma news release; 2018 May 21

June 11, 2018

Amgen recently announced that the US Food and Drug Administration (FDA) has approved the use of Prolia (denosumab) for the treatment of glucocorticoid-induced osteoporosis (GIOP) in men and women at high risk of fracture, defined as a history of

Week ending June 17, 2018

1. Lack of Sleep, Transition to SLE, May Be Linked
2. Remission, Low Disease Activity Compared in SLE

Denosumab

- Denosumab is a reasonable drug to prescribe, in the prevention and treatment of GIOP.
- Its use is particularly relevant in patients who have contraindications or side effects from bisphosphonates or anabolic therapy.

Denosumab in the treatment of GIOP: DovePress Drug Design, Development and Therapy 2019:13

Raloxifene

- Avoided in patients with SLE who have thrombotic tendency or history of vascular thrombosis.
- A small RCT in SLE patients has shown that raloxifene improved lumbar spine BMD without causing disease flares, this study excluded patients with hypercoagulability or anti-phospholipid syndrome.

ACR ,GIOP guidline

Take Home message

- The clinical management of GIOP, however, remains suboptimal .
- While bisphosphonates are currently the most widely used bone protective drugs in individuals taking glucocorticoids, the use of teriparatide and of denosumab as first-line options in some patients merits further investigation.
- Finally, the potential for sclerostin inhibitors to prevent or reverse adverse skeletal effects of glucocorticoids provides an exciting prospect for future research.


Our vision is a world without fragility fracture
in which healthy mobility is a reality for all.