



# WGO-OMGE 实践指南

## 骨质疏松症与胃肠道疾病

### Osteoporosis and gastrointestinal diseases

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## 1. 定义

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骨质疏松症是一种以低骨量和骨组织微结构破坏为特征，导致骨折危险性增加的全身性疾病。(1,2).

临床工作中胃肠病学家经常会遇到骨质疏松/低骨量的患者，建立一套诊断、表现以及治疗的指南将非常有帮助。

缩写:

BMD	骨盐密度	Bone mineral density
CD	克罗恩病	Crohn's disease
DXA	双能 X 线吸光测定法	Dual-energy x-ray absorptiometry
FIT	骨折干预试验	Fracture intervention trial
FSH	卵泡刺激素	Follicle stimulating hormone
GCS	糖皮质激素	Glucocorticosteroids
GGT	$\gamma$ 谷氨酰转移酶	Gamma glutamyl transferase
GI	胃肠道	Gastrointestinal
HRT	激素替代治疗	Hormone replacement therapy
IBD	炎症性肠病	Inflammatory bowel disease
LH	黄体生成素	luteinizing hormone
NSAID	非甾体类抗炎药	Non-Steroidal Anti-Inflammatory Drugs
PBC	原发性胆汁性肝硬化	Primary biliary cirrhosis
PSC	原发性硬化性胆管炎	Primary sclerosing cholangitis
PTH	甲状旁腺素	Parathyroid hormone
SERMs	选择性雌激素受体调节因子	Selective estrogen receptor modulators
SD	标准差	Standard deviation
UC	溃疡性结肠炎	Ulcerative colitis

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## 2. 流行病学

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概述:

- 30 岁时达到骨量峰值
- 骨骼成熟后, 骨量以每年 0.5 – 1.0% 的速度减少
- 女性绝经后 3-5 年有一骨量快速丢失期
- 随年龄增加骨密度逐渐减少, 骨折危险性增加
- 骨质疏松性骨折发生率随年龄增加而显著增高, 尤其是 60 岁以上的老年人。

骨质疏松性髌部骨折的严重性:

- 80% 发生于 65 岁以上的女性
- 骨折后 1 年的死亡率增加约 24%
- 髌部骨折死亡危险性与乳腺癌相近——两者均随年龄增加而增加
- 克罗恩病患者容易发生骨质疏松性椎骨骨折, 并进一步导致生活质量下降, 慢性疼痛, 日常活动能力受损, 社会活动减少, 用药增加和死亡率的增高

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## 3. 骨质疏松症与胃肠道/肝脏相关疾病

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### 3.1 炎症性肠病 (IBD)

- 克罗恩病与溃疡性结肠炎的骨盐密度降低发生率各家报道不一, 约占 IBD 患者的 25% (3,4,5,6)。
- 糖皮质激素应用是其发生的重要原因(7,8)
- 在 IBD 患者中, 骨盐密度降低可导致骨折发生率增加 40%
- 未使用糖皮质激素的 IBD 患者每年骨量丢失 3%, 而使用者每年丢失 6% (男女危险性相同)
- 长期糖皮质激素应用者骨折发生率高达 30-50%
- UC 患者骨量减少/骨质疏松的发生率和病变程度较 CD 患者低
- 骨代谢加快 (6)
- 与 CD 患者不同, UC 患者疾病诊断明确时骨质疏松症通常尚未发生, 主要见于激素应用者

### 3.2 糖皮质激素 (GCS)

- GCS 使用者的骨盐密度代表了骨折危险程度。服用 GCS 的类风湿性关节炎患者骨折相对危险性增高: 髌部, 2 倍; 脊椎, 4—5 倍
- 使用 GCS 第一年骨量丢失最快, 腰椎与股骨颈相似
- 导致骨质疏松症的 GCS 剂量阈值为 7.5 mg/天

### 3.3 乳糜泻

- 骨盐密度减少发生率为 30%, 25% 并发骨质疏松的口炎性腹泻患者发生外周骨骨折 (7,10)
- 钙与维生素 D 的吸收障碍, 甲状旁腺素 (PTH) 增高

### 3.4 肝脏疾病

慢性肝病，尤其是胆汁淤积性肝病患者骨生成减少，骨吸收增加 (11,12)。

与骨盐密度减少相关的肝脏疾病：

- 胆汁淤积性肝病：原发性胆汁性肝硬化（PBC），原发性硬化性胆管炎（PSC）
  - 10-60% 发生骨量减少/骨质疏松
  - GCS/熊去氧胆酸在骨质疏松发生中的作用机制尚未阐明(13,14)
- 血色病
- 酗酒
- 自身免疫性肝炎（包括 GCS 的应用）
- 肝移植
  - 起初的骨盐密度减少可能与 GCS/环孢菌素 A（CyA）/tacrolimus 的应用相关
  - 肝移植后 1 年内 20% 患者发生骨折

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## 4. 病因学

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与骨质疏松症相关的胃肠道因素：

- 常见的危险因素（年龄、性别、酒精摄入、吸烟）
- 口炎性腹泻
- 慢性肝脏疾病
- 炎症性肠病
- GCS 应用
- 胃/肠切除
- 胰腺功能不全
- 吸收不良

表 1：发生骨质疏松的危险因素：

- 原发性：与其他疾病或药物无关  
继发性：女性，40%；男性，60%
- 个人史
  - 40 岁以后的骨折史
  - 痴呆引起摔倒次数增加
  - 一般情况差/虚弱（偏瘫、四肢瘫、类风湿）
- 遗传
  - 一级亲属的髌、腕或脊椎骨折史
  - 性别
  - 老年
  - 高加索人种

- 生活方式
  - 吸烟
  - 过量酒精或咖啡因摄入
  - 久坐的生活方式
  - 长期低日光照射
- 内分泌
  - 绝经
  - 雌激素不足
  - 性腺功能减退
  - 甲状腺功能亢进
  - 甲状旁腺功能亢进
  - Cushing** 综合症
  - 厌食症
- 营养
  - 钙和维生素 D 缺乏
  - 生长发育期骨盐密度峰值低下
  - 低体重指数
  - 营养不良
  - 减肥时未控制的反复节食
  - 神经性厌食
- 药物长期应用
  - GCS**
  - 抗惊厥药
  - 肝素
  - 抗肿瘤药物
  - CyA / tacrolimus**

骨质疏松和骨折潜在的可逆危险因素:

- 已知低骨盐密度
- 体重低下
- 由以下原因所致的雌激素不足:
  - 过早绝经 (<45 岁)
  - 双侧卵巢切除
  - 延长的绝经期前闭经 (>6 个月)
- 钙摄入不足
- 营养不良
- 应用 **GCS** (至少 7.5 mg 强的松/天; 或等量其他激素类药物; 至少 3 月); 或内源性皮质醇增多症
- 酗酒
- 吸烟
- 咖啡因
- 反复摔倒
- 日光照射不足
- 体力活动不足
- 视力减退

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## 5. 诊断

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### 5.1 骨质疏松症的诊断:

- 有胃肠道疾病等危险因素的患者为疑似病例
- DXA 法测定骨盐密度
  - 金标准(16)
  - DXA (双能X线吸光测定法,  $\text{g}/\text{cm}^2$ )
  - Z-评分 – 与同年龄、种族、性别人群比较
  - T-评分 – 与同性别, 同种族的青年人骨量峰值比较
- DXA 诊断骨质疏松症的 WHO 指南: 骨盐密度下降超过 2.5 个标准差或者较青年平均值明显下降 (17)
  - 骨量减少是指 T-评分较平均值低 1 到 2.5 标准差
  - 老年患者, Z-评分将患者骨密度与同年龄, 种族, 性别的对照组比较

### 5.2 骨质疏松症合并胃肠道/肝脏疾病的诊断:

- 胃肠道/肝脏疾病的诊断及治疗
- Ca,  $\text{PO}_4$ , 25 羟-维生素 D, 碱性磷酸酶, ALT 或 AST
- 甲状腺功能检查
- 甲状旁腺素水平
- 性腺功能减退
  - F = 雌二醇与 LH/FSH
  - M = AM (早晨) 游离睾酮与总睾酮/性激素结合球蛋白; LH/FSH
- DXA 扫描: 治疗 1–2 年后复查

### 5.3 胃肠病学家进行骨密度测量的指征

- 具有发生骨质疏松危险性的胃肠道/肝脏疾病
- GCS 使用者
- 50 岁或以上的绝经后女性, 较绝经后危险因素超过 1 个或更多
- 65 岁或以上女性, 无论危险因素多少
- 有骨折表现的绝经后女性

DXA 复查的频率:

- 通常间隔 12–18 个月
- 评估骨折的危险性, 制定个体化的诊疗计划
- 若无行 DXA 检查的条件, 高危患者需经验性治疗

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## 6. 骨质疏松症的治疗

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## 6.1 推荐临床治疗方案：

明确患者是否使用类固醇激素，以及是否为绝经后骨质疏松非常重要：

1. 使用类固醇激素	二膦酸盐，其他药物二线
2. 无类固醇激素使用但有脆性骨折史	首选二膦酸盐或 raloxifene，其他药物二线
3. 无类固醇激素使用，无骨折史，无血管收缩症状	首选二膦酸盐或 raloxifene，其他药物二线
4. 无类固醇激素使用，无骨折史，有血管收缩症状	HRT, 其他药物二线(除 raloxifene – 加重血管收缩症状)

如果没有上述药物，治疗的关键是增加维生素 D 的摄入和日光照射量。日光照射量低的地区需在牛奶或其他食物产品添加维生素。

## 6.2 重要的药物治疗方案：

重要的药物治疗方案：

- 激素替代治疗 HRT
- 选择性雌激素受体调节因子 SERMS
- 降钙素
- 甲状旁腺素(PTH)
- 二膦酸盐
- 联合治疗

HRT 的作用机制仍不明确，考虑到长期用药存在发生妇科/乳腺肿瘤的潜在危险，必须谨慎用药。骨盐密度增加 5%，骨折危险性随之下降 50%。绝经期前开始 HRT 且持续 10 年以上，可取得最好的治疗效果，并可预防绝经后应用糖皮质激素治疗的女性患者骨量减少。

选择性雌激素受体调节因子(SERMS)治疗可使椎体骨折率（并非髌）下降 50%(28, 29)，SERMS 对雌激素水平低下的男性患者同样有效。

骨质疏松后降钙素治疗可降低椎体性骨折危险性，但对非椎体性骨折无效；降钙素治疗特别适用于绝经 5 年以上的女性以及一线药物治疗失败或者不能耐受的患者。

PTH 治疗骨质疏松症非常昂贵，只适用于重度患者(T-score < 3.5)

二膦酸盐应用于骨代谢增加的患者，尤其是绝经后骨质疏松与 GCS 相关性骨质疏松。

## 6.3 不同类型患者的治疗方案

### 6.3.1 绝经后女性的治疗：

- 钙剂 (1500 mg/天),维生素 D (800 IU/天)  
加  
药物治疗 (26)\*
- 雌激素（保留子宫的患者联合孕激素），尤其是有症状的女性 (27)

或

- 选择性雌激素受体调节因子 (raloxifene 60 mg./天)

或

- 二膦酸盐(阿仑膦酸 10 mg/天 或 70 mg/周, 或 risedronate 5 mg/天) \* 若有指征, 不需常规用药

### 6.3.2 GCS 相关性骨质疏松症的治疗:

二膦酸盐治疗 GCS 相关性骨质疏松症患者。

已证实三种二膦酸盐均能降低糖皮质激素性骨质疏松的骨折率, 而雌激素无效, 目前尚无数据显示 raloxifene 有效。

### 6.3.3 长期服用 GCS 患者的治疗:

- 初始评估
- 物理治疗
- 患者教育

表 2:

DXA: T score $\geq$ -1 $\rightarrow$ HRT	DXA: T score $<$ -1 $\rightarrow$ HRT 仅用于绝经后女性
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载自: ACR Task Force on Osteoporosis Guidelines (37,38).

### 6.3.4 长期服用 GCS 且有骨质疏松性骨折患者的治疗:

- 初始评估
- 物理治疗
- 患者教育

表 3

DXA: T score $\geq$ -1 实验室检查正常	DXA: T score $\geq$ -1 实验室检查异常	DXA: T score $<$ -1 实验室检查正常	DXA: T score $<$ -1 实验室检查异常
钙剂 & Vit D 补充	强化物理治疗	钙剂 & Vit D 补充	强化物理治疗
HRT	治疗潜在病因	强化物理治疗	治疗潜在病因
强化物理治疗	钙剂 & Vit D 补充	HRT	钙剂 & Vit D 补充
HRT			

载自: ACR Task Force on Osteoporosis Guidelines (37,38)

二膦酸盐的主要胃肠道副作用为:

- 食管炎: 烧心, 吞咽困难, 吞咽痛

- 胃/十二指肠溃疡

## 6.4 预防

### 6.4.1 一般预防

下列生活方式改变有助于预防骨质疏松症：

- 减少过量酒精、咖啡因摄入、减少吸烟
- 达到理想体重
- 保持适量体育锻炼的计划
- 对消化不良的患者保证足够的钙剂与维生素 D 的摄入，控制预防高钙血症或高尿钙

表 4： GCS 相关性骨质疏松症的预防与治疗：

临床治疗	1 级预防	2 级预防 & 治疗
如可能，减少 GCS 用量	✓	✓
钙剂& 维生素 D	无	✓
Calcitrol	✓	-
二膦酸盐	✓	✓
激素替代治疗	-	✓
降钙素	✓	✓
氟化物	±	✓

## 6.5 发展中国家指南：

- 第三世界的主要骨代谢疾病为骨软化症/佝偻病，由于营养不良，以及文化或者宗教实行全身衣物遮盖所致。
- 治疗关键是增加钙剂与维生素 D 的摄入，增加日光照射

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## 8. Useful websites and consensus statements

### 1. American College of Rheumatology:

<http://www.rheumatology.org/>

- Fact Sheet: Osteoporosis and Corticosteroid-induced osteoporosis:  
<http://www.rheumatology.org/public/factsheets/osteopor.asp>
- Treatment of Steroid-Induced Osteoporosis ACR Task Force on Osteoporosis Guidelines : <http://www.rheumatology.org/publications/guidelines/osteo/osteo.asp>

### 2. European Foundation for Osteoporosis

<http://www.connect.ie/effo/index.htm>

### 3. International Osteoporosis Foundation

<http://www.osteofound.org/>

- Position Papers and Guidelines  
[http://www.osteofound.org/publications/position\\_papers\\_guidelines.html](http://www.osteofound.org/publications/position_papers_guidelines.html)

### 4. National Institutes of Health – Osteoporosis & Related Bone Diseases National Resource Center

<http://www.osteoporosis.org/>

- Research Bibliographies: <http://www.osteoporosis.org/research.asp>
- NIH Consensus Statement:  
Osteoporosis Prevention Diagnosis and Therapy:  
[http://odp.od.nih.gov/consensus/cons/111/111\\_intro.htm](http://odp.od.nih.gov/consensus/cons/111/111_intro.htm)

#### 5. National Osteoporosis Foundation (USA)

<http://www.nof.org>

- Osteoporosis Clinical Practice Guideline:  
<http://www.nof.org/professionals/clinical/clinical.htm>

#### 6. National Osteoporosis Society (UK)

<http://www.nos.org.uk/>

- Position Statements for Health Professionals: <http://www.nos.org.uk/healthprof.asp>

#### 7. Osteoporosis Australia

<http://www.osteoporosis.org.au/html/index.php>

- Position Papers: <http://www.osteoporosis.org.au/html/healthpapers.php>

#### 8. Scottish Intercollegiate Guidelines Network (SIGN)

<http://www.sign.ac.uk>

- Management of Osteoporosis, No. 71  
<http://www.sign.ac.uk/pdf/sign71.pdf>

#### 您的问题和反馈

诊治指南委员会欢迎您的任何评论和问题。您认为我们忽略了某些方面吗？您感到有些操作是否有额外的危险？告诉我们您的经验。点击下面的按钮让我们知道您的观点。让我们一起做得更好。

