

Bone health in menopausal women: a role for General Practitioners

Raffaella Michieli¹
Martina Musto²

¹ "SIMG" National Secretariat, Venezia, Italy

² General Practitioner, Venezia, Italy

Address for correspondence:

Raffaella Michieli

"SIMG" National Secretariat

Venezia, Italy

E-mail: michieli.raffaella@simg.it

Summary

General Practitioners (GPs) are in a prime location to assess patient health needs, knowing clinical history, living habits and risk factors. GPs can identify in healthy people those in which prevention could be useful, in order to avoid or delay some diseases. For this purpose GPs need to change their care model from a *waiting model* to a *proactive model*, in order to identify health needs before the development of diseases.

KEY WORDS: risk factor; FraHS; supplements; menopause.

What should be evaluated in over 50-year-old menopausal women?

Lifestyle and familiarity. GP should periodically evaluate patient's habits that could compromise health, paying particular attention to smoking, alcoholic drinking, physical exercise, diet, familiarity for cardiovascular diseases, cancer, osteoporosis and hip fractures.

Cardiovascular risk. Cardiovascular problems (ischemic heart disease, stroke and other heart diseases) are the main cause of mortality in developed countries. In Europe cardiovascular diseases are accountable for 48% of all deaths, but mortality is higher in women (54%) (1). The protective role of estrogens for atherosclerotic disease is well known, but in post-menopausal women cardiovascular risk grows and becomes similar to that of men at the age of 75. Many scores are available to calculate cardiovascular risk: European score (SCORE) calculates risk for fatal event in the next 10 years considering age, sex, smoking, blood pressure and cholesterol blood level; Italian score (CUORE) calculates risk for fatal and non fatal event in the next 10 years considering age, sex, diabetes, smoking, blood pressure and cholesterol blood level. Evaluations of smoking, blood pressure, weight, blood cholesterol and blood sugar should be executed in menopausal women.

Cancer prevention. In Italy three screening programs are

available: searching occult blood loss in stool of over 50 years aged men and women for early diagnosis of bowel cancer; mammography in over-50 women for early diagnosis of breast cancer; pap test in women over 25 years for early diagnosis of cervix cancer. GP should make sure of patients' access to screening programs and invite them to do it.

Menopausal symptoms. Menopausal symptoms should be investigated in order to establish if hormonal treatment is necessary. Hot flushes are the most frequent, but other symptoms are often reported: they are mood changes, sleep disturbance, memory impairment, loss of sexual desire and vaginal dryness, headache, genitourinary disorders, muscle and joints pain. When symptoms are slight, estrogen treatment should be considered, in the absence of contraindications.

Hormone replacement therapy

The decision to start an estrogen treatment in menopausal woman should be made through the analysis of risks *versus* benefits. Probably the risks more likely associated with HRT (i.e. breast cancer, increasing cardiovascular risk, venous thromboembolism) are due to long term (> 5 years) or too late started therapy (2, 3). The indications for an estrogen therapy are:

- treatment of severe menopausal symptoms
- prevention and treatment of osteoporosis in women with high risk of fracture, when they can't use usual therapy for osteoporosis.

The stronger contraindications are: unknown uterine bleeding, breast or endometrial cancer, venous thromboembolism, coronary or cerebrovascular diseases and liver diseases.

Fracture risk: role of General Practitioner

Fragility fractures, especially hip fractures, considerably affect morbidity and mortality, so GP's essential task is to identify those patients at risk of osteoporosis and fracture and to stratify their risk. GP also deals with making a correct diagnosis and setting an appropriate therapy. For this purpose, the first step is to identify risk factors as early menopause, low weight (BMI \leq 19), smoking, alcohol abuse, familiarity for fracture or severe osteoporosis, low calcium intake, history of premenopausal amenorrhea, diseases or therapies leading to loss of bone mass. A correct and complete registration of clinical records is needed, where it should be possible to calculate fracture risk and to take the most appropriate diagnostic and therapeutic decision: the role of each risk factor is so complex that specific algorithms are needed. There are many algorithms available to predict probability to develop hip fracture or other major fractures in the following 10 years: FRAX®, developed by Centre for Metabolic Bone Disease of University of Sheffield, is the most used and known. De-

FRA® is an algorithm derived from FRAX® developed on Italian population.

The Italian Society of General Practice and Primary Care Professionals (SIMG) developed a new algorithm based on its own database Health Search whose data are particularly accurate and representative of Italian population: FraHS (4). This new algorithm offers the big advantage of calculating fracture risk without BMD data, because it's based only on risk factors; it provides the fracture risk for 5 and 10 years with a good predictive power, and suggests if the patient needs therapy. There is a medical record used by GPs in Italy, which includes this algorithm, thus allowing an immediate evaluation of the fracture risk. Parameters used by FraHS are listed in Table 1.

Table 1 - Risk factors used in FraHS.

Age
Sex
History of fragility fractures
Smoking
BMI
Alcohol abuse
Glucocorticoids use
Chronic diseases associated with loss of bone mass

Once the risk is assessed, GP needs to decide if a measurement of BMD could be necessary by execution of a DXA. This can be useful especially when in doubt about therapeutic choice. Italian Ministry of Public Health established access criteria to DXA: no evidence of the use of DXA as widespread screening is available, so it should not be prescribed in the absence of risk factors or when BMD value is not essential to establish a therapy. DXA can be used as a diagnostic confirmation in case of fractures by mild injuries, and it is offered in presence of one of higher risk factors or three of lower risk factors (Tables 2, 3).

Prevention and therapy

Prevention is a key approach including promoting healthy lifestyle (quit smoking, avoid alcoholic drinks, exercise regularly), recommending higher intake of dairy products, water rich in calcium and lower intake of salt. GPs can also check any condition leading to falls (5) (Table 4).

Table 2 - Access to DXA, higher risk factors.

Male and female of all ages	Menopausal female
- History of fractures or radiological evidence of spine fractures	- Maternal family history of osteoporotic fracture before 75 years
- Radiological evidence of osteoporosis	- Menopause after 45 years
- Chronic diseases associated with loss of bone mass	- BMI ≤ 19
- Chronic therapies associated with loss of bone mass	

Table 3 - Access to DXA, lower risk factors.

Age > 65
Family history of severe osteoporosis
History of premenopausal amenorrhea
Low calcium intake
Lack of vitamin D
Smoking
Alcohol abuse

Table 4 - Risk factors for falls.

Individual factors
History of previous falls
Conditions impairing:
- Muscle mass/strength (sarcopenia)
- Lower limb function
- Balance
- Vision
Cognitive impairment
Arrhythmias
Drugs (acting on CNS, anti-hypertensives, alcohol)
Muscle impairment due to hypovitaminosis D
Environmental factors
Barriers, lighting, floor, shoes

Supplementation of calcium and vitamin D is not needed in all people, even if lack of vitamin D is very common in Italy, especially concerning elderly people during winter months. In younger patients (< 60 years aged) a widespread screening of lack of vitamin D and its supplementation is not suggested (6). However in those patients with risk factors, dosing blood calcium and vitamin D could be useful. Calcium intake through diet should be preferred to other calcium supplementations (5). Concerning vitamin D, oral administration route on a daily or weekly basis should be preferred; dose has to be adjusted on serum vitamin D level (5). Adequate calcium and vitamin D intake is essential with all pharmacological approaches; three class of drugs are available in Italy whose access is regulated by NOTA AIFA 79:

- Antiresorptive drugs: bisphosphonates, SERMs, denosumab
- Drugs stimulating bone anabolism: teriparatide
- Dual-acting drugs: strontium ranelate.

Denosumab, teriparatide and strontium ranelate can be prescribed only by specialists. GPs can prescribe only bisphosphonates and SERMs.

Furthermore, pharmacological treatment is supported by SSN only in the following conditions:

- A. *Secondary prevention* in patients with history of osteoporotic fractures
- Spine or hip fractures
 - Other fractures and T score (lumbar or femoral) ≤ -3
- B. *Primary prevention* in menopausal women or men over 50 years, with high risk of fracture because of one of the following conditions:
- Treatment (ongoing or planned) for at least 3 months with prednisone $\geq 5\text{mg/die}$ (or other glucocorticoid in equivalent dose)
 - Adjuvant treatment with hormonal blockers in women with breast cancer and men with prostatic cancer
 - T-score (lumbar or femoral) ≤ -4
 - T-score (lumbar or femoral) ≤ -3 and the presence of one of these conditions at least:
 - Familiar history of hip or spine fracture
 - Comorbidities associated with fracture risk (rheumatoid arthritis or other connectivities, diabetes, COPD, BID, AIDS, Parkinson's disease, multiple sclerosis, movement impairment).

According to the previous criteria, this kind of therapy can rarely be prescribed in women if menopause is the only risk factor. However, in presence of any risk factor, a supplementation of vitamin D should be considered. Although HRT proved to have a favorable effect on fracture, a long term treatment is not recommended because of the increased risk of breast cancer, cardiovascular diseases, thromboembolism and dementia. In presence of severe menopausal symptoms the need of HRT should be considered for a limited time, especially in women between 50-55 years, when contraindications don't exist. After publication of WHI study, HRT prescription decreased and many women were excluded from a therapy they could have taken advantage of; furthermore they often refuse HRT fearing side effects. In those women at risk of fracture reporting moderate menopausal symptoms,

use of soy isoflavons, vitamin D and lactoferrin supplements can be evaluated. Soy isoflavons seem to improve vasomotor symptoms, mood changes and sleep disturbances acting on temperature control hormones and serotonin. Many findings about lactoferrin as a regulator of bone cell activity are available: *in vitro* lactoferrin stimulates proliferation and differentiation of osteoblast-like cells, prevents apoptosis in osteoblast-like cells, stimulates chondrocyte proliferation and inhibits osteoclastogenesis and increases bone growth *in vivo* (8).

Conclusions

Menopause should be considered a chance for health. In a woman reporting amenorrhea or climacteric symptoms an overall assessment of lifestyle and risk factors should be done. Prevention of fragility fractures is a basic task because of their negative impact on morbidity, mortality and quality of life: GPs are in a strategic position for identifying people at risk and choose the appropriate preventing and therapeutic strategy.

References

1. European Heart Network "Statistiche delle malattie cardiovascolari in Europa 2008".
2. Menopausa e Terapia Ormonale Sostitutiva. BIF N°6 Nov-Dic 2001.
3. SNLG ISS. Linee guida menopausa della Regione Toscana. 2015.
4. Lapi F, et al. Assessing Risk of Osteoporotic Fractures in Primary Care: Development and Validation of the FRA-HS Algorithm. *Calcif Tissue Int*. DOI 10.1007/s00223-016-0230-7.
5. Rossini M, et al. Guidelines for the diagnosis, prevention and management of osteoporosis. *Reumatismo*. 2016;68(1):1-39.
6. Adami S, et al. Guidelines on prevention and treatment of vitamin D deficiency. *Reumatismo*. 2011;63(3):129-147.
7. Sommella C, et al. Evaluation of the efficacy of dietary supplements based on Equisetum arvense, soy isoflavones, lactoferrin and vitamin D3 on the control of climacteric symptoms. *Italian Journal of Gynaecology & Obstetrics*. 2015;27(2).
8. Cornish J, et al. Lactoferrin is a potent regulator of bone cell activity and increases bone formation in vivo. *Endocrinology*. 2004;145(9):4366-4374.