

MECHANISM-BASED APPROACHES TO THE ANALYSIS OF COMPARATIVE EFFECTIVENESS IN OSTEOPOROSIS

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Abstract

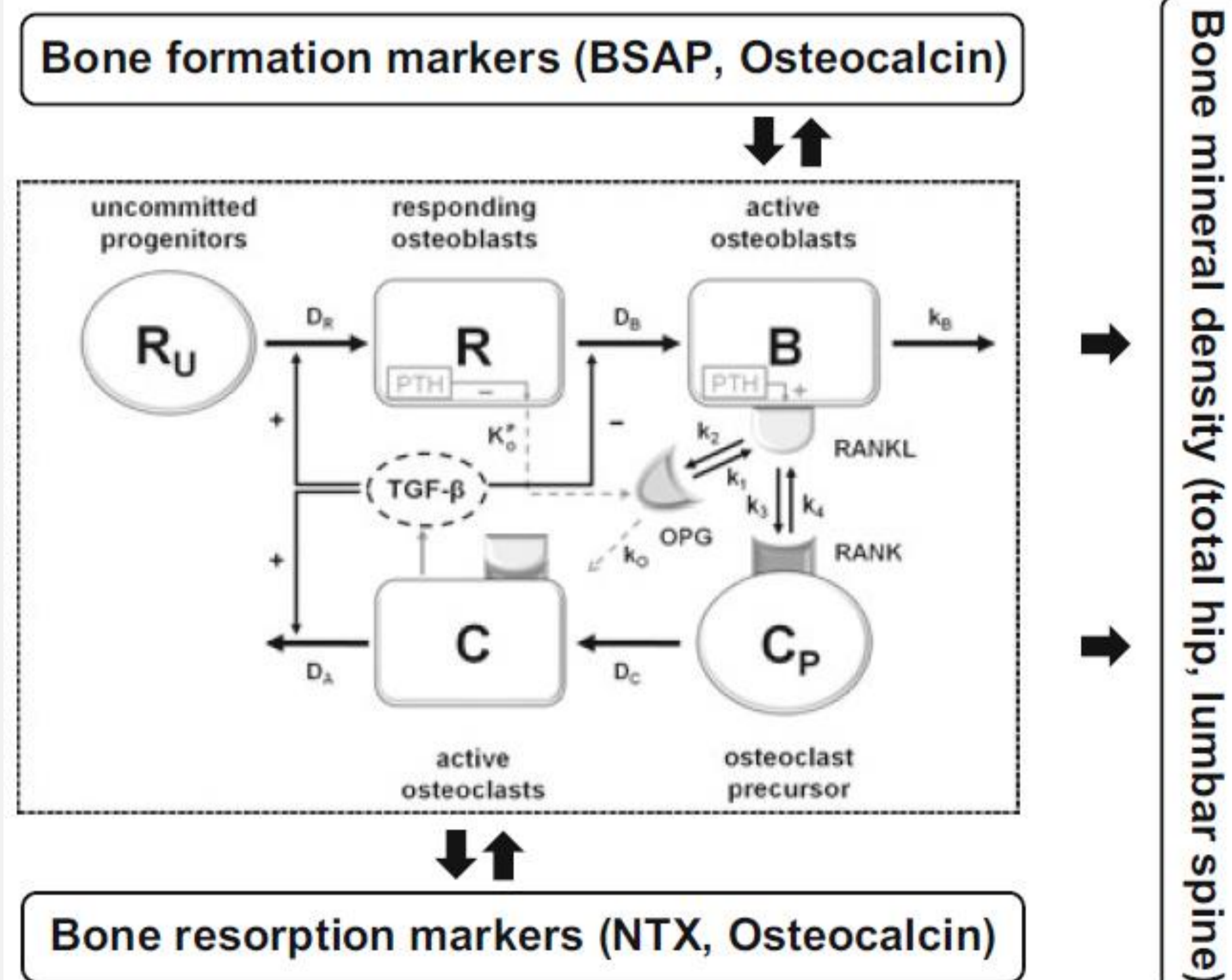
Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Recently, a mechanistic osteoporosis framework was developed to describe disease progression together with treatment effects. This model was applied to clinical data from post-menopausal women receiving various doses of tibolone or calcium [1]. In this study we aim (i) to apply the mechanistic model to treatment with various doses of alendronate and (ii) use a population cohort study (The Rotterdam Study) to describe whether variations in bone mineral density in the real-life population is due to treatment effects or to other covariates.

Tibolone data

“Prevention of bone loss with tibolone in postmenopausal women: results of two randomized, double-blind, placebo-controlled, dose-finding studies [2].”

Mechanistic model

“Application of a mechanism-based disease systems model for osteoporosis to clinical data [1].”



References

1. Post TM et al. (2013) *J Pharmacokinet Pharmacodyn.* 40(2):143-56.
2. Gallagher JC et al. (2001) *J Clin Endocrinol Metab.* 86(10):4717-26.
3. Ravn P et al. (1999) *Ann Intern Med.* 131(12):935-42.
4. Hofman A et al. (2014) *Eur J Epidemiol.* 28:889-926

Application of mechanistic osteoporosis network to alendronate treatment

Comparative analysis

Clinical trial data

- 1518 postmenopausal women receiving placebo or different doses of alendronate (2.5 or 5.0 mg/daily) for four years [3].
- Measurement of biomarkers (BSAP & UNTX) and bone mineral density (BMD) at the lumbar spine and total hip every 6 months.
- Women in the alendronate groups received alendronate for the first 2 years. Treatment was then continued without change or replaced with placebo for the last 2 years of the study.

Real-life population

- Prospective cohort study started in 1990 in suburb of Rotterdam [4].
- 10994 men and women aged 55 over
- Investigate prevalence and incidence of risk factors for chronic diseases in elderly.
- Baseline measurements (including, BMD, fractures, (co-)medication and comorbidity) between 1990-1993, subsequent examination for follow-up rounds every 2-3 years.

Study objectives

- ✓ Study the difference between the efficacy observed in clinical trial and the real-life effectiveness.
- ✓ Addressing disease progression as well as the impact of demographic and other factors on the effectiveness of osteoporosis treatments.
- ✓ Extend the current mechanistic osteoporosis framework with fracture data available from the real-life population.