OSTEOSCAN

PARTNERS IN OSTEOPOROSIS MANAGEMENT

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Osteoscan remains South Australian and doctor- owned "of clinicians, by clinicians, for clinicians". We hope that this newsletter is of interest and welcome your feedback and support by way of referrals.

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Welcome to another exciting year of bone density testing at Osteoscan. We hope that you will find some useful take-home messages in this annual newsletter. We will be expanding our reporting pool in 2019 with several younger hyper-talented endocrinologists, so look out for the names on your reports. New Hologic machines have been installed at Marion and Kurralta Park. The detail of the clinical notes provided to us continues to increase exponentially, posing some very challenging clinical questions. If you don't agree with the answers/comments please let us know.

Best Wishes for 2019 from Team Osteoscan!

Capture the fracture

We would all view unstable angina as a clear call to urgent intervention to prevent more serious cardiovascular events. It has been understood for some time that the risk of further cardiovascular events is very high in the short term in such patients. Although it is widely known that having had one fragility fracture essentially doubles the risk of another such fracture, unfortunately it appears that many doctors do not appreciate the short time frame within which this second fracture is likely to occur. Subsequent fracture risk is not constant, but fluctuates over time. The risk of subsequent vertebral, hip, and nonvertebral non-hip fractures is highest immediately after initial hip, clinical, and radiographic vertebral fractures and nonvertebral fractures and declines afterward, regardless of gender, age, and initial fracture location. These data indicate the need for early action after an initial fracture with medical interventions that have an effect within a short term to reduce the preventable risks of subsequent fractures.

For example, after a hip fracture the relative risk for a second hip fracture was 11.8 at 1 month, decreasing exponentially to 3.0 at 6 months and 2.2 at 1 year, and did not normalise until after 15 years. Looking at it another way, after clinical fracture (i.e. symptomatic) of the hip, vertebrae or shoulder, 34% of all subsequent fractures (hip, clinical vertebral, forearm, or shoulder) during a follow-up of 5 years, occurred within the first year after the initial fracture and progressively decreased to 9% during the 5th year. The time to act to prevent subsequent fractures is now.

The messages which have been endorsed by the International Osteoporosis Foundation based on these and other data are clear:

Osteoporosis is a common disease: It is estimated that worldwide, a fragility fracture occurs every three seconds.
One fracture leads to another: Having suffered a prior fragility fracture almost doubles a patient's future fracture risk.
Fractures are warning signs: Half of patients presenting with hip fractures have suffered a prior fracture.
We fail to 'capture' the first fracture: The majority of fragility fracture patients are neither assessed, nor treated by their health care system to reduce fracture risk.
The Care Gap: To achieve a significant reduction in future fracture rates and resulting healthcare costs, healthcare systems must target those patients who have already suffered a fracture, as they are the ones at highest risk for future fractures.

So, next time you see a patient who has sustained a fragility fracture, think of them as having "unstable bones". Consider starting specific treatment early, and do not delay appropriate investigations which will usually include an Osteoscan and a vertebral fracture assessment. The fractured wrist that causes your patient so much pain and inconvenience could also be the early warning that helps you prevent them from being institutionalised or even dying as a result of a hip fracture. Don't delay – capture the fracture!

The Fasting serum Crosslaps

For the last eight years at Osteoscan, we have recommended measurement of fasting serum Crosslaps. A recent publication in Osteoporosis International has underlined the importance of this practice in the follow-up of patients who have commenced therapy with oral bisphosphonates.The authors reviewed the use of two markers: P1NP (a marker of bone formation) and Crosslaps (CTX, a marker of bone resorption).

> **"The working group recommends measuring P1NP and CTX at baseline and three months after starting therapy to check for a decrease above the least significant change (decrease of >38% for P1NP and >56% for CTX). Detection rate [of nonadherence to therapy] is 87% for CTX, and 94.5% if both are measured.**
>
> **"If a significant decrease is observed the treatment can continue but, if no decrease occurs, the clinician should reassess to identify problems with treatment, mainly low adherence."**

It is essential to underline to patients that they **must be fasting prior to the test**. Any consumption of food or nutritious drinks will suppress the level of Crosslaps (and, to a lesser extent, P1NP).

There are four other circumstances in which we have found that measurement of fasting serum Crosslaps is useful.

- When screening patients, measurement of Vitamin D and Crosslaps is a simple and cheap strategy that may lead on to useful discoveries.
    - A low level of Crosslaps (say, below 150 nmol/L) may draw attention to the fact that the patient has omitted to mention recent antiresorptive therapy; or may identify a low turnover state – for example in chronic renal disease.
    - A high turnover state may prompt further screening tests, such as ALP, PTH, TFT, serum and urine electrophoresis; or – if extremely high – imaging for Paget's disease or metastases or myeloma.
- When planning the next date for repeat measurement of BMD, we recommend shorter intervals in post-menopausal women with elevated Crosslaps, because accelerated bone turnover (Crosslaps above 450 or especially above 600 ng/L according to unpublished data from Chris Nordin) is associated with more rapid bone loss and an increase in fracture risk.
- An annual measurement of Crosslaps in patients on oral bisphosphonates may recognise those who have ceased to adhere, or are not taking their medication according to instructions.
- The recently recognized condition of Rebound-associated vertebral fractures after denosumab discontinuation is of great concern and may be associated with high CrossLaps. In six patients who discontinued denosumab for more than 12 months and who were not covered with bisphosphonate the median CrossLaps was 1190. When assessing a patient previously prescribed denosumab, but uncertain of timing of last injection, it is suggested that a CrossLaps be measured to exclude the possibility of severe bone turnover rebound.

Vitamin D controversies

In June 2017 an international panel of experts was assembled to discuss controversies in the field of Vitamin D. Australia was well represented. A report has just been published in the February edition of JCEM. Several of the issues are highlighted below. Mostly this is not new information, but will hopefully serve to underpin your existing clinical practice.

A Vitamin D of 50 – 125 nmol/L is regarded as safe and sufficient for skeletal health in the healthy general population. However, it is not known if this range can be applied to patients with osteoporosis or primary hyperparathyroidism.

Vitamin D supplementation at 800 IU daily has been shown to reduce fracture incidence in the elderly (>70 years), patients with Vitamin D deficiency and in aged care settings. This is most likely to be due to improved muscle function and reduced falls, as opposed to a direct effect on bone.

Regarding extra-skeletal effects of Vitamin D, there is a consistent association between poor Vitamin D status and obesity and Type 2 diabetes. This reflects the fact that Vitamin D is predominantly stored in fat. However, Vitamin D supplementation does not prevent diabetes or influence any component of the metabolic syndrome. The clinical consequence is that higher doses of Vitamin D for longer will be required to achieve sufficiency in overweight/obese individuals.

Replacement of Vitamin D using high loading doses has been previously shown to increase fracture risk. This has now been extended to monthly bolus dosing regimens which were associated with increased risk of falls and fracture. This is a common practice and it is suggested that it be replaced by a daily dosing regimen.

In primary hyperparathyroidism 25OH Vitamin D is often low and associated with higher indices of disease activity, as in bone turnover markers or rate of loss of bone. There is a role for careful supplementation to decrease PTH production so as to improve bone outcomes. This might be relevant in cases where one is pursuing a strategy of observation rather than surgical referral. Care is needed not to provoke hypercalcemia or hypercalciuria.

Glucocorticoids inactivate Vitamin D by inhibiting it's hepatic and renal hydroxylation, lowering the active form 1,25 diOH Vitamin D. Consideration could be given to the use of calcitriol to prevent steroid-induced osteoporosis. This is not a new concept and in 1993 Australian researchers showed that calcitriol was effective in preventing loss of BMD at the spine in steroid-treated patients, but even when combined in a meta-analysis fracture prevention was not demonstrated.