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Biochemical markers of bone turnover: Useful but underused

Biochemical markers of bone turnover are commonly used as tests in the management of bone disorders, as explained very elegantly by Drs. Singer and Eyre in this issue of the *Journal*.[1]

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These tests assess the activity of osteoblastic cells or osteoclastic cells in a variety of bone diseases. Such tests do not establish the diagnosis of a disease, but rather they reflect the activity of the skeleton. Because the activity of osteoblasts and the activity of osteoclasts are chemically coupled, markers of blastic and clastic activity move in the same direction. In states of high bone metabolism or turnover, marker levels are high, predicting bone loss and fracture risk. Therapies that slow down bone metabolism make these levels decrease; anabolic drugs that stimulate bone growth do the opposite.

The utility of these markers in general practice is not well appreciated. In part this is because the results can vary if the tests are not appropriately done, causing frustration for some clinicians, who erroneously conclude that these markers lack utility.

WILL INSURANCE PAY FOR TESTING?

In addition, these tests are a source of confrontation with third-party payers who refuse to pay for them, even though they are approved by Medicare and have appropriate Current Procedural Terminology codes assigned to them. The reasons cited for denying payment are that the tests are not diagnostic, that they do not predict risk, and that they are not useful in patient management.

Wrong on all counts! First of all, these markers were never meant to diagnose a specific bone disease. They reflect high bone activity or turnover and potential bone loss, and high levels indicate that further assessment is needed. (In much the same way, an elevated prostate-specific antigen level may or may not mean the patient has prostate cancer, but it does mean further assessment is needed.)

Second, these tests do address fracture risk, either when used alone or when combined with bone densitometry measurements. A high level of a turnover marker indicates a risk of fracture similar to that of a T score lower than –2.5, with an odds ratio in the range of 2.4 to 2.8.[2] Moreover, if a patient has a low T score *and* a high marker level, his or her risk is even higher, with an odds ratio of 4.1.

Markers tell us the risk of fracture and are useful in patient management

Third, the argument about the tests' lack of ability to help in patient management is completely untrue, as shown by information reviewed by Drs. Singer and Eyre,[1] and by other data recently published.[3] These tests can indicate whether bone physiology is responding to antiresorptive and anabolic drug therapy: marker activity should decline with antiresorptive drugs and increase with anabolic agents.

And this occurs months to years before bone densitometry even reflects a change! The failure of test values to respond appropriately should prompt physicians to find out why. Is the patient not taking the medicine appropriately? Or more worrisome, is he or she not taking it at all?

AN ADDED BENEFIT: BETTER ADHERENCE

The latter point brings up a common problem seen in practice—lack of adherence to drug

therapy. Studies have repeatedly shown that only 50% to 60% of osteoporotic patients actually continue taking their oral medicine for a year or so.[4,5] The reasons are unclear but may include cost, side effects, inconvenience in administration, and lack of any sign that the drug is doing anything. Bone densitometry may not always show changes that encourage patients to continue using expensive medicines.

Bone markers may be a solution to this dilemma. Changes in a bone marker help clinicians know that the patient is properly using therapy.[6] Moreover, these changes tell the *patient* that treatment is working. In my experience, relaying this type of information to the patient encourages adherence. Studies have indicated that markers do indeed help patients stay adherent to therapy and avoid fractures.[7,8] Hence, these markers can indicate the risk of fracture and are useful in managing patients and promoting compliance.

It is unclear when third-party carriers will begin reading the appropriate literature to confirm these points, but practitioners need to recognize that there is a valid reason for using these tests.

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