Peripheral Versus Axial Skeleton Absorptiometry in Osteoporosis

TO THE EDITOR: In their letter of November 1985, Vogel and Wasnich (1) posit a similarity of single-photon absorptiometry (SPA) of the peripheral skeleton and dual-photon absorptiometry (DPA) of the axial skeleton for diagnosis and monitoring of osteoporosis. They contrast these nuclear medicine procedures to quantitative computed tomography (QCT), which they deem to be less cost-effective. In doing so, however, they neglect to mention research which has shown that direct measurements of osteoporotic fracture sites (hip and spine) are needed to define fracture risk. Many investigators in osteoporosis research no longer believe the peripheral skeleton can be used as an indicator of the axial skeleton. Numerous reports have shown that measurements at sites like the distal radius and os calcis show a standard error of estimate of 15% in predicting axial density in normals (2). The 95% confidence interval in bone disease ranges from 25 to 50%. The study of Nilas et al. (3) confirmed this. In a recent review of methods by the American College of Physicians (4) DPA and QCT were selected as preferred methods. In regard to effectiveness DPA, QCT and other (albeit experimental) methods measuring the axial skeleton share more in common than they do with peripheral measurements.

Readers must note that the conclusions of Vogel and Wasnich regarding the os calcis are based on their unique, and as yet unreplicated, study (5) of 26 nonosteoporotic fractures (including six wrist, eight rib, ten foot/lower leg). The authors were able to generate a monotonic relationship of fracture rate to os calcis density but this relationship was critically dependent on a few fracture cases. There is no evidence that os calcis density is superior to body weight, let alone site-specific density, for spine or hip fractures. This same study showed that all fracture cases were below the “fracture threshold” of 1.0 g/cm² for spinal density (or 2 s.d. below the mean in normal U.S. whites) while half of the fracture cases had normal os calcis density (above 275 mg/cm³). Thus the spine was a better discriminator of risk than peripheral sites, even for these nonosteoporotic fractures. The os calcis is particularly suspect because it is so dramatically influenced by body weight and physical activity. Even if os calcis measurements could predict long-bone fractures, there would be no basis for extrapolating to hip and spine fractures since peripheral fractures, including Colles fractures of the distal radius, are unrelated to those of the axial skeleton (6,7). In contrast measurement of the spine, by either DPA or QCT, directly reflect fracture risk; fracture rate increases as density decreases (8).

We agree that a screening procedure for osteoporosis that can be broadly applied, at low-cost, is needed. However, all studies on peripheral skeletal sites show a high proportion of false negatives (9), particularly in younger patients where preferential axial osteopenia has not yet been reflected by generalized skeletal loss (10). In their own study of spinal osteoporosis (11) the Hawaiian investigators found that the os calcis was not more sensitive than the distal radius or the radius shaft. All these sites exhibited over 50% false negatives (9), particularly in younger patients where spine or hip fractures. This same study showed that all fracture cases were below the “fracture threshold” of 1.0 g/cm² for spinal density (or 2 s.d. below the mean in normal U.S. whites) while half of the fracture cases had normal os calcis density (above 275 mg/cm³). Thus the spine was a better discriminator of risk than peripheral sites, even for these nonosteoporotic fractures. The os calcis is particularly suspect because it is so dramatically influenced by body weight and physical activity. Even if os calcis measurements could predict long-bone fractures, there would be no basis for extrapolating to hip and spine fractures since peripheral fractures, including Colles fractures of the distal radius, are unrelated to those of the axial skeleton (6,7). In contrast measurement of the spine, by either DPA or QCT, directly reflect fracture risk; fracture rate increases as density decreases (8).

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References


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REPLY: Noronha has measured the distribution of technetium-99m (99mTc) glucoheptonate in various organ systems in a rat model. His results are similar to those obtained by Arnold et al. in 1975 using a rabbit model (1). While this group did not examine the small bowel in this phase of their study, they did report a value of 0.25% for that organ in a dog model.

Numerous studies attest to the efficacy of [99mTc]glucoheptonate in the evaluation of renal function. The radiopharmaceutical is admirably suited for this purpose if reasonable precautions are observed as pointed out by us (2) and Noronha. However, we find it difficult to agree with his statement that glucoheptonate should not be used for brain scanning because of the radiation dose to the kidneys and GI tract. Glucoheptonate has been shown to be superior to [99mTc]diethylenetriaminepentaacetic acid for the detection of intra-cranial pathology (3) making it the agent of choice for brain scanning.

References

References


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REPLY: We are pleased to have this forum to respond to the arguments presented by Dr. Mazess. The primary point of our letter may have been missed. We proposed that the clinical uses of BMC measurements should be well defined before comparisons between techniques are conducted. We indicated that monitoring of treatment effectiveness is one important clinical use, and the precision is an essential requirement, measurement of multiple bone sites by all three techniques (QCT, DPA, and SPA) may have usefulness for this purpose. We also suggested that assessment of future fracture risk was another important clinical application, and that for this purpose the priorities are different. As a screening test, it must be safe and cost effective, and it must also be predictive of future fracture risk.

Therein lies the root of this apparent dispute. How is “fracture risk” to be defined? In his letter, Dr. Mazess has only referenced studies based upon fracture prevalence data (i.e., fractures that occurred at some, often unknown, time in the past). These fractures were then compared to subsequent BMC measurements. By definition, these studies tell us how well the BMC measurements assess past fracture risk. It is our contention that there is little need in clinical medicine for a new test that identifies subjects with previous fractures; virtually all such cases can be identified by proper histories and conventional radiographs. We suggest that what is really needed is a test which will identify, at an early age (40–50 yr), which women are at greatest risk for fractures in the future, and who would therefore benefit from preventive therapy. In this particular context, attempts to relate BMC at one skeletal site to BMC at another site are not relevant. Rather, it is the relationship of BMC to clinical outcome (i.e., future fractures) that is needed. In order to determine whether any risk factors, including BMC, are indicative of future fracture risk, they must necessarily be compared to prospective fracture incidence. There is virtually no such data in the medical literature.

Our data has been inaccurately paraphrased. [The reader is referred to the original manuscript for an unabridged version (1).] We agree that it does challenge “conventional wisdom,” but contend that prevalence fractures, which constitute much of the existing data, are inappropriate for assessment of future fracture risk. Consideration of this disease as two discrete variables, i.e., “fracture” vs. “nonfracture” is also inappropriate analysis, since BMC is a continuous variable which relates to a continuum of risk.

Dr. Mazess states that research has shown that direct measurements of osteoporotic fracture sites (hip and spine) are needed to define fracture risk.” Is that true? Has that hypothesis been tested against prospective fracture incidence, using all possible skeletal BMC measurement sites? The answer is no. However, like many hypotheses in medicine, its apparent reasonableness, has transformed it into a fact in some minds. It should also be noted that “osteoporotic fractures” cannot be arbitrarily limited to hip and spine. All nonviolent fractures occur more frequently in osteopenic bone, and therefore cannot be ignored. In addition, fractures at some sites, particularly wrist, may be indicative of increased subsequent risk for fractures of the spine and hip (2,3).

We have been testing the above hypothesis in a longitudinal, population-based cohort. We are including multiple appendicular and axial BMC measurements precisely because none have been appropriately tested, particularly within the same cohort. We now have some preliminary data which challenges this hypothesis. Although this is certainly preliminary data and will require further followup, it is appropriate to collect and report such data. During the past 5 yr more than 20,000 individual scans have been performed on this cohort of 3,000 individuals. To date there are 150 prevalence fractures and 50 incidence fractures available for analysis of relative risk. We have more recently presented an analysis of incidence fractures which included a substantial proportion (40%) of spine fractures (4). Although the data do suggest that future spine fracture risk can be assessed with spine BMC measurements, there is an equally good relationship for os calcis BMC. For appendicular fractures, os calcis and radius BMC were superior to spine BMC as predictors. Thus, at this time, based upon preliminary analyses of our data, we have concluded that prediction of fracture risk at a given skeletal site, such as spine, does not necessarily require direct BMC measurement at that site. By way of analogy, prediction of stroke risk with blood pressure measurements, as employed in a physicians
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