What's the Skinny on Bone Health for People With HIV?

Researchers have called for revised treatment guidelines to address the higher risk of fracture in the HIV population.

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Bone mineral density (BMD) loss alone doesn't explain why people with HIV have a higher rate of bone fractures compared with the general population. Considering this along with the various established ways of mitigating the risk of broken bones, including therapies to treat and prevent osteoporosis and switching antiretroviral (ARV) regimens, the Danish authors of a new systematic review and meta-analysis recommend more proactive guidelines for preventing bone loss and fractures among HIV-positive individuals.

Along with cardiovascular disease (CVD), cognitive impairment and cancer, bone loss is among the numerous health challenges becoming increasingly important for people with HIV and their clinicians to focus on as the first generation of people living with the virus progresses into old age.

Jakob Starup-Linde, PhD, of the department of endocrinology and internal medicine at Aarhus University Hospital in Denmark, led a research team that conducted a systematic review of 142 published studies that compared fracture risk between people with and without HIV. The investigators also conducted a meta-analysis of 87 of those papers. Their findings were published in the Journal of Acquired Immune Deficiency Syndromes.

Compared with HIV-negative control subjects in the studies analyzed, people with HIV had a 1.5-fold increased risk of any fracture and a fourfold increased risk of a fracture related to fragility—that is, bone breaks not caused by traumatic injuries.

Reductions in BMD, the study authors found, explained only 15% of the increased risk of fragility fractures. "These findings," they wrote, "underline a bone deficiency in PLHIV [people living with HIV] besides what is reflected in BMD."

In the studies included in the analysis, BMD was assessed at the hip, lumbar spine or both using dual-energy X-ray absorptiometry, otherwise known as a DEXA scan.

After HIV-positive study participants started ARV treatment for the first time, they experienced rapid declines in BMD. During the first year, this decline was comparable between those taking

tenofovir disoproxil fumarate (TDF), the older version of tenofovir, versus those taking regimens that do not include that drug. However, during the second year of treatment, the decline in BMD stabilized in people with HIV as a whole, while among those on TDF, there was a 0.67% decline at the lumbar spine and a 0.35% decline at the hip.

TDF, sold under the brand name Viread, is also used as a treatment for hepatitis B virus (HBV). The drug is included in the ARV combination tablets Atripla, Complera, Delstrigo, Symfi, Symfi Lo, Stribild, Cimduo and Truvada. It has long been established that TDF is associated with declines in BMD as well as detrimental change in biomarkers associated with kidney function. Nevertheless, because of the drug's otherwise high level of tolerability as well as low toxicity and high potency compared with other ARVs in its drug class, TDF was for many years the most commonly prescribed HIV medication.

Gilead Sciences, which manufactures TDF, has in recent years rolled out a new version of the drug, called tenofovir alafenamide (TAF), which is associated with lower bone loss as well as improved kidney health. TAF, which is sold under the brand name Vemlidy as an HBV treatment, is included in the Biktarvy, Genvoya, Odefsey, Symtuza and Descovy combo tablets.

Recently, another group of researchers conducted an analysis of 11 trials and found that TAF's bone-related superior safety over TDF was significant only when TAF and TDF were paired with a "booster," either Tybost (cobicistat) or Norvir (ritonavir). (Boosters are medications that have no therapeutic function but boost the levels of other ARVs in the blood.)

Nevertheless, the new systematic review and meta-analysis found that over 48 weeks, treatment with TAF or abacavir (sold as Ziagen and included in the Triumeq combo pill) was indeed superior to TDF in terms of preservation of BMD. (This analysis did not differentiate those outcomes based on whether individuals took a booster.) The gap in bone loss progression between TDF and TAF continued to widen through 96 weeks of treatment and then stabilized through 144 weeks. As for TDF versus abacavir head-to-head, the difference in BMD seen at 48 weeks remained stable through 96 weeks of treatment.

"Other factors than HIV may explain the increased fracture risk in PLHIV," the study authors noted. They pointed to the high rate of HBV and hepatitis C virus (HCV) coinfections among people with HIV and noted that each hepatitis virus has been established as independently associated with an increased risk of bone fractures.

"Awareness of osteoporosis in hepatitis B– or C–coinfected PLHIV is therefore warranted," the investigators concluded.

Possibly because of the reduction in muscle mass that the virus can cause, people living with HIV are also at an increased risk of falls as they age, which may in turn put them at risk of fractures. Fall-driven fractures in old age in turn put people at an elevated risk of developing frailty, which itself puts indiviudals at high risk of death.

Osteoporosis treatments, the review and meta-analysis indicated, can have a significant impact on

BMD in people with HIV. The drug alendronate (Fosamax), for example, increased BMD at the lumbar spine by 3.5%, although its effect on the hip was unclear.

While there has been less research into zoledronate (Reclast), available evidence indicates that its BMD-boosting effects among people on ARVs can last through seven years of follow-up. A single dose of that drug neuralized the decrease in BMD that people starting ARVs for the first time otherwise would have experienced.

Among those taking TDF, zoledronate provided better protection against BMD loss compared with switching to a regimen that did not contain that ARV.

In response to an additional analysis they conducted of numerous global guidelines for bone care among people with HIV, the paper's authors urged more prompt diagnosis and treatment of osteoporosis in this population. Driving their concern was the fact that the increased rate of fractures seen in HIV-positive people compared with their HIV-negative peers starts at a relatively young age. The overall disparity is only expected to widen as increasing numbers of individuals with the virus surpass age 60. Additionally, among those study participants with the virus who were younger than 40, their BMD percentage decrease over time was similar to the rate of decline seen in their older counterparts.

Given how the BMD of people with HIV as well as their FRAX score—a standard measure of osteoporosis-related fracture risk—underpredict their risk of fractures, the paper's authors recommended that osteoporosis prevention for this population should possibly begin when individuals have a T-score higher than -2.5. (A T-score indicates the density of an individual's bones compared with the density of those of a healthy 30-year-old.)

The paper's authors made a comparison to the stepped-up bone-health prevention efforts that are recommended for people treated with glucocorticoid medications. As is apparently the case with HIV, glucocorticoids such as hydrocortisone or prednisone increase the risk of fracture beyond what reductions of BMD are expected to do. For individuals taking glucocorticoids, osteoporosis treatment is recommended when they have a T-score of just -1.0 or -1.5.

The authors also recommended that HIV primary care include routine DEXA scans and that health care providers offer their patients information about how to promote healthy bones through lifestyle choices. Such bone health–promoting behaviors include quitting smoking, reducing the use of alcohol, eating a healthy diet that includes sufficient calcium and vitamin D and exercising regularly. Physicians should also screen for risk factors associated with falls, including low blood pressure after standing up (orthostatic hypotension).

For those age 40 or older with a T-score at the spine or hip below -1.5, the researchers suggested switching off of regimens that contain TDF. If there are other fracture risk factors, zoledronate or alendronate treatment to prevent osteoporosis should be initiated. Zoledronate, in particular, is not just more effective at treating bone loss compared with switching ARVs, it also doesn't need to be taken routinely like alendronate and thus doesn't run the risk of being compromised by an individual's lack of adherence to the regimen.

“In conclusion,” the study authors wrote, “fracture risk is increased in PLHIV and is not sufficiently explained by BMD reduction. New fracture predictors are needed in PLHIV, and BMD and bone microarchitecture should be investigated further. As the fracture risk is increased, we recommend optimization of current guidelines with earlier initiation of osteoporosis prophylaxis and treatment.”

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