Perspective

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Metabolic Dysfunction-Associated Steatotic Liver Disease and Bone Health Risk

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Description

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a common chronic condition that affects approximately 25% of the global population. This disease includes various liver disorders characterized by excessive fat accumulation, which can progress from simple steatosis (fatty liver) to Metabolic Dysfunction-Associated Steatohepatitis (MASH) and in severe cases, cirrhosis. The development of MASLD is driven by multiple mechanisms, including insulin resistance, disrupted lipid metabolism, oxidative stress, low-grade inflammation, altered gut microbiota and increased intestinal permeability. MASLD is closely associated with several comorbidities, such as type 2 diabetes mellitus (T2DM), obesity and cardiovascular diseases. Recent studies suggest that MASLD may also adversely affect bone health, leading to both quantitative and qualitative changes that increase fracture risk.

Research, including systematic reviews and meta-analyses, has established a link between MASLD and osteoporosis, as well as osteoporotic fractures, in both children and adults. Factors such as chronic low-grade inflammation, altered adipokine and hormone levels and vitamin D deficiency have been proposed as mechanisms through which MASLD impacts bone health. However, the relationship between MASLD and changes in Bone Mineral Density (BMD) remains contentious, likely due to variations in study populations, designs and the heterogeneity of MASLD itself. Therefore, there is a pressing need for further longitudinal studies with diverse cohorts to clarify these associations.

MASLD and BMD in children and adolescents

Bone mineral density reflects the amount of minerals in bones and is a important indicator of fracture risk. The T-score compares a patient's BMD to that of healthy young individuals of the same sex, with a score of -2.5 or lower indicating osteoporosis. Conversely, the Z-score compares BMD with peers of the same age and sex, with a Z-score of -2.5 or lower suggesting secondary osteoporosis.

As the prevalence of obesity, T2DM and MASLD increases among children and adolescents, recent research indicates that these young individuals may have lower BMD. For instance, a meta-analysis involving 632 children demonstrated that those with MASLD had lower BMD compared to their non-MASLD counterparts, with the severity of MASLD correlating with reduced BMD. Another analysis focused on 453 obese adolescents reported similar outcomes. While most studies indicate that MASLD negatively affects BMD in youth, some findings suggest that simple steatosis may not significantly impact BMD, whereas MASH likely does. A cross-sectional study in Korea, however, found no significant differences in BMD Z-scores across different groups, highlighting the necessity for additional investigation.

MASLD and BMD in adults

A considerable body of research has explored the connection between MASLD and reduced BMD in adults. A 2019 meta-analysis analyzed data from over 30,000 individuals, concluding that there was no significant correlation between BMD at various skeletal sites and MASLD. Nevertheless, it identified an increased likelihood of osteoporotic fractures in those with MASLD, particularly among older Chinese men, suggesting that while MASLD may not drastically affect bone quantity, it could influence bone quality.

A subsequent meta-analysis conducted in 2023, surround a larger sample size, found that MASLD was associated with a heightened risk of osteoporosis and osteoporotic fractures, particularly within Asian populations, while no such association was evident in non-Asian groups. Cohort studies generally corroborate the link between MASLD and lower BMD, with women often exhibiting more pronounced effects than men. Some studies have reported that MASLD, particularly MASH, correlates with decreased BMD, while conflicting results from other studies indicate a complex relationship influenced by factors such as race, sample size and MASLD severity.

MASLD and fragility fractures

Emerging evidence suggests a significant association between MASLD and osteoporotic fractures. For example, a large cross-sectional study found that MASLD with fibrosis correlated with a higher likelihood of major osteoporotic and hip fractures, particularly in men aged 50 and older. Another nationwide study indicated that individuals with MASLD faced a greater fracture risk compared to non-MASLD controls. Gender differences have

also been observed, with some studies suggesting a stronger association in men, while others report no significant differences.

Metabolic dysfunction-associated steatotic liver disease presents a multifaceted challenge, not only as a chronic liver condition but also as a potential contributor to compromised bone health. The existing literature highlights a complex and nuanced relationship between MASLD and bone mineral density, with evidence suggesting that while the disease may not consistently impact BMD quantity, it likely affects bone quality and increases the risk of osteoporotic fractures.