## RESEARCH HIGHLIGHTS

## **OSTEOARTHRITIS**

## Gait abnormalities, bone mineral density and subchondral bone loss in knee OA

The presence and incidence of subchondral bone attrition (SBA) in knee osteoarthritis (OA) is associated with joint malalignment, but not with low bone mineral density (BMD), according to new research published in the *Annals of the Rheumatic Diseases*.

"Although bone abnormalities are known to exist in OA," explains Tuhina Neogi, the lead author of the paper, "the focus of OA research has remained largely on understanding why and how cartilage abnormalities occur". As a step towards clarifying the role of bone in OA, the investigators undertook the present work to examine the potential influence of bone quality and abnormal loading on SBA, a type of bone abnormality observed in OA (Figure 1). The group had previously shown that "cartilage loss tends to occur in the same subregions of a knee as SBA, which suggests that one might influence the other, or that a common factor, such as focal loading, influences the occurrence of both in the same location," says Neogi.

The cross-sectional, 30-month observational study was undertaken as part of the Multicenter Osteoarthritis (MOST) study, which includes a large cohort of participants who have or are at high risk of developing OA. At baseline, 550/1,253 (44%) of the knees studied had radiographic OA and SBA was present in 416/1,253 (33%). Full-leg radiography revealed varus malalignment in 612/1,253 (49%) and valgus malaligment in 249/1,253 (20%) of the knees, and 392/1,253 (31%) were neutrally aligned. The analyses were adjusted for age, sex, and body mass index, and the use of bone-modulating medications was also taken into account.

The results showed that tibiofemoral joint alignment is associated with both baseline and incident SRA, consistent with other evidence of a relationship between focal loading and knee OA. At baseline, valgus malalignment was associated with

SBA in the lateral compartment (odds ratio [OR] 4.5, 95% CI 2.8–7.1) and varus malalignment with medial-compartment SBA (OR 2.9, 95% CI 2.1–4.0). Over the study period, the incidence of SBA in the lateral and medical compartments was significantly associated with baseline valgus and varus deformities, respectively (ORs 2.1, 95% CI 1.1–4.1 and 1.9, 95% CI 1.2–2.9).

Further analyses limited to those knees without radiographic OA at baseline revealed similar effects of malalignment on the incidence of SBA in each compartment, although these associations did not reach statistical significance,

To determine whether the occurrence of SBA could be related to bone turnover, systemic BMD—as measured by dualenergy X-ray absorptiometry—was used as a rough measure of bone quality. Contrary to the investigators' expectations, low BMD was not associated with an increased incidence of SBA. Patients in the highest tertile of systemic BMD had SBA more often, both at baseline (OR 1.5, 95% CI 1.1-2.1) and over the 30-month study period (OR 1.6, 95% CI 1.1-2.3), than patients in the lowest tertile. Further analyses determined that the effect of baseline malalignment on the presence of SBA was not influenced by BMD. "This finding suggests that BMD could be a reflection of the overall load experienced through the knee joint over a lifetime," says Neogi, "and is in keeping with the association between higher BMD and knee OA".

The authors suggest that BMD is, therefore, "not a specific enough marker for abonormal bone turnover or bone quality". As Neogi explains, "To answer the question of whether bone quality predisposes to SBA, one would need to assess local bone quality." Tools such as micro CT and peripheral quantitative CT could prove valuable in such investigations.



**Figure 1** | MRI of a knee showing subchondral bone attrition on the medial femur (arrowhead) and medial tibial plateau (arrow).

Professor Linda Sandell of Washington University in the USA suggests that the results of the study provide a rational association between increased load on the bone and/or cartilage and a measurable outcome; namely, radiographic detection of bone loss. "This study demonstrates a clear association between specific malalignment and the development of site-specific, measurable bone attrition, and thus begins to connect abnormalities in gait with radiographic findings with an active cellular process."

The investigators intend to continue to work toward understanding the role of bone in OA, the inter-relationship between bone and cartilage abnormalities, and risk factors for such abnormalities. "As well," says Neogi, "our future work will continue to focus on the interaction between biomechanical and systemic factors that might play a role in OA."

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