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Advancing Opportunistic Detection of Osteoporosis Through AI-Driven CT Segmentation

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Introduction/Background
Despite DXA availability, osteoporosis remains significantly underdiagnosed. CT scans can be used for opportunistic screening of low bone density (LBD, bone mass density values at or below the osteopenia threshold). More than 80% of fragility fractures in women occur within the osteopenic range, indicating the importance of early detection. Our objective was to determine the utility of LBD opportunistic screening and phenotypic analysis using large-scale AI-segmentation of CTs from the Penn Medicine BioBank (PMBB).

Methods/Intervention
Data were obtained from PMBB, including EHR-linked imaging and laboratory data from consented patients in an IRB-approved protocol. CT scans from 11,615 unique patients were processed using TotalSegmentator to segment the L1 vertebra. Radiomic analysis of L1 was conducted using pyradiomics v3.0.1 to calculate attenuation in Hounsfield Units (HU), with attenuation < 190 HU defining LBD. For each Phecode in our PheWAS, conducted using the PheWAS R package, a logistic regression was fitted for LBD prediction, controlling for age and sex.

Results/Outcome
1403 patients had ICD codes for LBD present at any skeletal site. Our AI-based L1 segmentation identified 1731 patients with LBD. 409 patients had both an ICD diagnosis and AI-detected LBD. 1322 patients had only AI-detected LBD, while 994 had only an ICD diagnosis. L1 attenuation between men and women were more similar than expected. A PheWAS study showed that respiratory-related Phecodes had the strongest associations with LBD at L1. Respiratory failure, lung transplant, pleurisy, and pleural effusion displayed the highest positive correlations, followed by cardiovascular conditions including pulmonary heart disease, heart transplant, heart failure, ischemic heart disease, and atrial fibrillation/flutter.

Conclusion
LBD was underdiagnosed within the PMBB dataset, even with our L1-restricted screening. Expanding segmentation beyond L1 may further improve detection and reconcile the discrepancy between clinically-diagnosed and AI-detected LBD, especially since ICD codes for LBD at any skeletal site were included. Our PheWAS identified strong correlations between LBD and respiratory and cardiovascular disorders.

Statement of Impact
AI opportunistic screening holds promise to improve early detection of osteopenia and can guide efforts to better characterize phenotypic profiles of affected individuals. Our study supports automated CT analysis for uncovering undiagnosed osteoporosis, highlighting opportunities for further understanding associated

comorbidities.

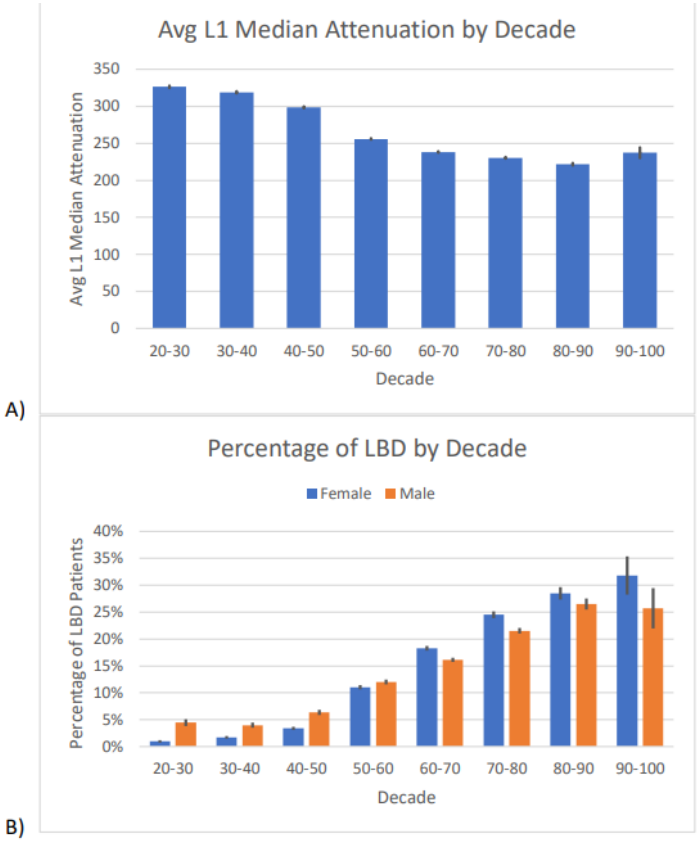

Figure 1: Average median attenuation of the L1 vertebra **(1A)** and sex-stratified percentage of LBD patients **(1B)** across age intervals in decades

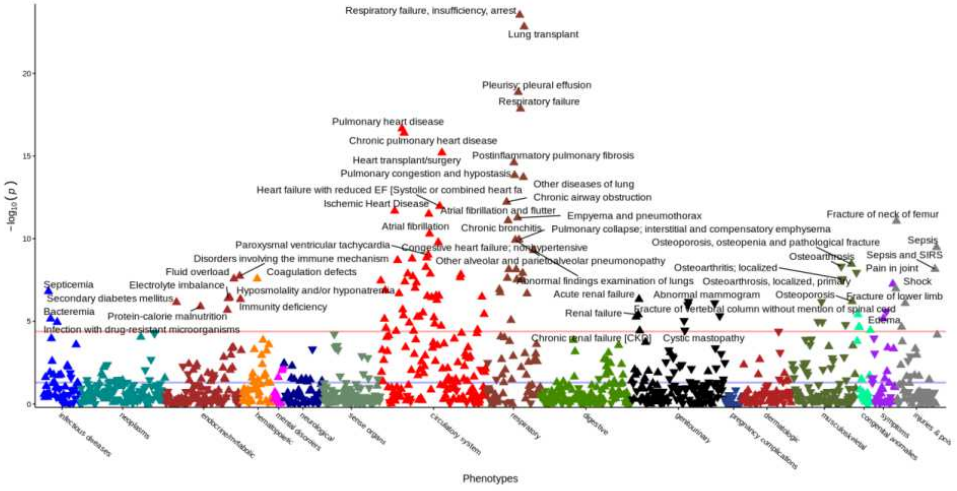

Figure 2: PheWAS of low bone density of the L1 vertebra. The blue line represents p=0.05; the red line represents the Bonferroni-corrected threshold at p=3.99 x 10^{-5}. Diagnoses above the red line demonstrate a statistically significant relationship with low bone density after multiple comparison testing.

Keywords

osteoporosis; CT segmentation; artificial intelligence; opportunistic diagnostics