Opportunistic detection of osteoporosis on low-dose chest computed tomography scans

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INTRODUCTION
Low bone mineral density (BMD) is a treatable but underdiagnosed condition. Associated low-trauma fractures contribute to significant morbidity and public health cost[2].

Low-dose chest computed tomography (LDCT), when performed for indications such as lung cancer screening, can be assessed opportunistically for vertebral fractures (VF) and vertebral BMD and thus facilitate early detection and intervention of osteoporosis in high-risk groups.

Clinical osteoporosis guidelines recommend combining BMD assessment (using gold-standard dual-energy X-ray absorptiometry [DXA] or quantitative CT [QCT]) and clinical fracture risk assessment to guide management. Validated clinical tools, such as the FRAX and Garvan models, can be used to estimate absolute risk of osteoporotic fracture[1].

The CT attenuation value of vertebral trabecular bone at L1 (L1HU) has been shown to correlate well with DXA[2]. In absence of DXA or QCT, it presents a simple yet objective method of BMD screening. While recall bias associated with clinical risk tools may be avoided, the predictive value of objective BMD measurements in classifying VF is unknown.

METHODS
In this prospective cohort study, baseline LDCT scans were performed in 595 International Lung Screening Trial participants between 2017 and 2019 at The Prince Charles Hospital (Queensland, Australia). A trained observer assessed CT images for BMD and VF.

Participants completed baseline questionnaires to ascertain fracture risk factors.

CT Bone Density Assessment Methods:

1) L1HU Method
Mean attenuation value (Hounsfield units) was measured from a single region of interest in the vertebral body of L1 using IntelliviewTM software [Fig 1a].

2) QCT Method
Average volumetric density (mg/cm³) of T12-L1 vertebral bodies was measured using Mindways QCTProTM software [Fig 1b].

Low BMD (including osteoporosis and osteopenia) was defined by L1HU <110HU[3] or QCT BMD <120mg/cm³[4].

Vertebral Fracture Assessment:
Prevalence of VF was assessed using the semiquantitative Genant scoring method[5] and was defined as having at least 1 ‘moderate’ or ‘severe’ VF (i.e. Genant score of ≥2, equivalent to ≥25% loss of vertebral height on CT) [Fig 1c].

Clinical Osteoporotic Fracture Risk Assessment:
FRAX and Garvan 10-year absolute osteoporotic fracture probability was calculated using clinical information obtained in questionnaires. ‘High risk’ was defined as a probability score ≥4% of hip fracture or ≥20% of other major osteoporotic fracture as per either tool[6].

Statistical methods:
We used receiver-operating curve (ROC) analyses and area under ROC (AUC) comparison to discriminate between methods, chi-square test to compare proportions and Wilson’s test to calculate confidence intervals for proportions.

RESULTS

• 36 participants were included in analyses after exclusion of those without complete questionnaire data or analysable scans. Descriptive statistics are shown in the table below.

<table>
<thead>
<tr>
<th>Total participants</th>
<th>Mean age (years)</th>
<th>Male</th>
<th>Low BMD</th>
<th>High Fracture Risk</th>
<th>Prevalent VF (OCT + Genant score ≥ 3)</th>
<th>L1HU &lt;110HU</th>
<th>L1HU ≥110HU</th>
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<tr>
<td>n (%) or M (SD)</td>
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<td>536 (100)</td>
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<td>188 (34)</td>
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• 56% (n=302) had low QCT BMD and 35% (n=188) had prevalent VF above severe VF.

• L1HU values showed excellent correlation with QCT (r=0.899) [Fig 2].

• L1HU classified low QCT BMD accurately (AUC 94.5%) [Fig 2], with specificity 95.7% and sensitivity 70.2% at a threshold <110HU.

• L1HU more accurately classified low QCT BMD (p<0.0001) compared to FRAX (AUC 66.9%) and Garvan scores (AUC 64.3%) [Fig 2].

• L1HU was superior to clinical risk scores in correctly classifying prevalent VF with AUC FRAX 49.1% (p=0.0003) and AUC Garvan 48.4% (p=0.0005) [Fig 3].

CONCLUSION

• VF and low vertebral BMD can be systematically quantified on LDCT scans.

• In doing so we found a high prevalence of both conditions among lung cancer screening participants.

• BMD measurement methods statistically outperformed validated clinical risk tools in classifying prevalent VF, however none of the methods tested achieved optimal accuracy in classifying prevalent VF.

• The L1HU method performed very well compared to gold-standard QCT and could be opportunistically applied to routine LDCT scans to accurately detect osteoporosis in high-risk groups.

FURTHER RESEARCH

• We will investigate the predictive accuracy of BMD measurement methods and clinical risk tools in predicting incident fracture over a 5 year follow-up period.

• We will aim to develop and validate a multivariable risk prediction model combining L1HU measures and key clinical factors to optimally predict incident fracture.

REFERENCES


ACKNOWLEDGEMENTS

• University of Queensland Thoracic Research Centre
• International Lung Cancer Screening Team
• The Prince Charles Hospital Thoracic Department