Association of CT-Measured Hepatic Steatosis with Quality of Life

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Introduction

Biological aging is characterized commonly by diminished physical function and the loss of muscle ("sarcopenia"), decreased bone density ("osteopenia"), and visceral fat accumulation ("visceral obesity"). Rather than acting independently, these physiological systems are now thought to be interrelated, at least in part owing to pro-inflammatory cytokines driving cellular senescence and the systemic effects of endocrine factors from muscle, bone, and fat.

Interrelationships between organ systems can be evaluated non-invasively with routine CT scans, and we have successfully measured these biomarkers in a very large, publically-available, longitudinal dataset curated by the National Institutes of Health (National Lung Screening Trial (NLST); www.cancer.gov). This dataset has not been exploited to analyze the relationship between metrics we have already measured at UCD (i.e., muscle, bone, visceral fat) and other important tissues (e.g., liver, spleen). Furthermore, these CT biomarkers have not been analyzed holistically to assess for associations with key clinical outcome measures available through the NIH – including **quality of life (QoL)**.

The most common cause of diffuse liver disease in the USA is nonalcoholic fatty liver disease (NAFLD). Although numerous studies have shown hepatic steatosis is associated with an increased risk of fatal and non-fatal cardiovascular disease[4], recent research suggests that hepatic steatosis is significantly associated with sarcopenia. Specifically, as liver disease worsens, the prevalence of sarcopenia rises, with 1 in 4 people with NAFLD having sarcopenia vs. 1 in 10 for people without liver disease (odds ratio of 2.8 after controlling for co-morbidities).

Hypothesis

We hypothesize that the CT assessment for hepatic steatosis is associated with activities of daily living and could improve risk stratification for predicting mortality in patients with sarcopenia, osteopenia, and/or visceral obesity.

Methods

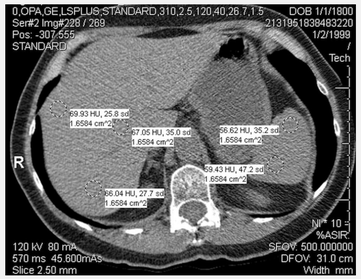
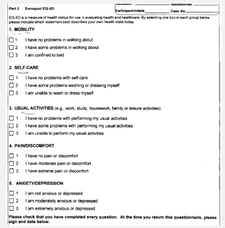


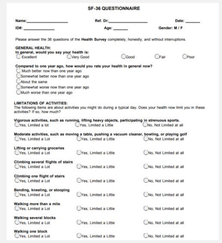
Figure 1: Axial CT scan shows liver and spleen attenuation (density) measurements

Analysis of baseline chest CT scans from all NLST participants age 70-74 years who had QoL data was performed.

Liver and spleen measurements were recorded using the single CT image at which the liver and spleen are optimally seen (**Figure 1**). Three equally spaced regions in the right lobe of the liver (>1cm^2) and two equally spaced regions of interest in the spleen (>1cm^2) were recorded, taking care to avoid large vessels, focal lesions, and image artifacts.



EQ-5D Questionnaire



SF-36 Questionnaire

QoL data was obtained from the NLST SF-36 and EQ-5D questionnaires. From SF-36, physical health component score (PCS) and mental health component score (MCS) were derived. From EQ-5D, a composite EQ Index as well as dichotomized self-reported mobility, self-care, and usual activities, pain/discomfort, and anxiety/depression metrics were derived.

The association between liver/spleen attenuation and QoL metrics was determined using multiple linear regression models for PCS, MCS, and EQ index and logistic regression models for binary outcomes, after adjusting for age and BMI.

Results

	Total (n=486)	Men (n=299)	Women (n=187)
Age	71.66 (1.37)	71.67 (1.34)	71.65 (1.43)
BMI	27.61 (4.48)	27.51 (3.74)	27.76 (5.45)
PCS	46.52 (9.14)	46.50 (9.09)	46.55 (9.25)
MCS	53.72 (8.77)	54.32 (8.21)	52.76 (9.54)
EQ Index	0.83 (0.13)	0.83 (0.14)	0.83 (0.12)
Liver (HU)	62.23 (9.06)	62.12 (8.80)	62.40 (9.47)
Spleen (HU)	52.88 (4.09)	53.38 (4.10)	52.08 (3.95)
L-S Ratio	1.18 (0.19)	1.17 (0.17)	1.20 (0.20)

Table 1: Participant characteristics

	SF-36: Physical Health	SF-36: Mental Health	EQ Index
Liver (HU)	β= -0.562 (p=0.290)	β= 0.180 (p=0.713)	β= 0.002 (p=0.813)
Spleen (HU)	β= 0.336 (p=0.521)	β= -0.102 (p=0.833)	**β= 0.002 (p=0.031)**
L-S Ratio	β= -0.646 (p=0.230)	β= 0.246 (p=0.612)	β= -0.001 (p=0.213)

Table 2: Association of CT attenuation and QoL metrics in men

486 participants (299 men, 187 women; mean age, 71.7 years; mean BMI 27.6) were analyzed (**Table 1**). Using EQ-5D, limitations in mobility were reported in 32.1%, limitations in self-care in 2.9%, and limitation in usual activities in 25.0% of participants.

In men: EQ index was positively correlated with spleen attenuation when adjusted for age and BMI (p=0.0313), but not with liver attenuation or L-S ratio. Self-reported pain was associated with spleen attenuation when adjusted for age and BMI (p=0.0056). No significant associations between PCS/MCS and L/S were observed (**Table 2**).

In women: QoL metrics were not associated with liver attenuation, spleen attenuation, or L-S ratio when adjusted for age and BMI

Limitations

The NLST took place at multiple sites and involved different CT equipment, making reproducibility of imaging difficult to attain. Best efforts were made to measure CT attenuation consistently, but reproducibility of measurement is a potential methodological limitation.

Future investigators may consider a longitudinal study design to assess changes in QoL alongside compositional changes in the liver and spleen.

Conclusions

In older men, higher spleen CT attenuation values were associated with higher quality of life, as measured by the EQ-5D Questionnaire. There were no significant associations between liver/spleen attenuation and any of the SF-36 metrics evaluated in this study.

In older women, there were no significant associations between liver/spleen CT attenuation and quality of life.

References

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