Review Article on Implementation of CT-based Screening of Lung Cancer

Added benefits of early detection of other diseases on low-dose CT screening

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Abstract: Low-dose CT screening for lung cancer provides images of the entire chest and upper abdomen. While the focus of screening is on finding early lung cancer, radiology leadership has embraced the fact that the information contained in the images presents a new challenge to the radiology profession. Other findings in the chest and upper abdomen were not the reason for obtaining the screening CT scan, nor symptom-prompted, but still need to be reported. Reporting these findings and making recommendations for further workup requires careful consideration to avoid unnecessary workup or interventions while still maximizing the benefit that early identification of these other diseases provided. Other potential findings, such as cardiovascular disease and chronic pulmonary obstructive diseases actually cause more deaths than lung cancer. Existing recommendations for workup of abnormal CT findings are based on symptom-prompted indications for imaging. These recommendations may be different when the abnormalities are identified in asymptomatic people undergoing CT screening for lung cancer. I-ELCAP, a large prospectively collected multi-institutional and multi-national database of screenings, was used to analyze CT findings identified in screening for lung cancer. These analyses and recommendations were made by radiologists in collaboration with clinicians in different medical specialties.

Keywords: Health check; ancillary findings; lung cancer; chronic obstructive pulmonary disease (COPD); cardiovascular disease; breast

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Introduction

Low-dose CT (LDCT) screening is approved for reimbursement by insurance companies and the Centers for Medicare and Medicaid Services (CMS) in the United States since 2015 (1). A study sponsored by the National Institutes of Health and The Bill and Melinda Gates Foundation found that between 1990 and 2016, ischemic heart disease, lung cancer, and chronic obstructive pulmonary disease (COPD) are the top three killers in the United States (2) and also worldwide (3).

LDCT, while screening for lung cancer, also

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provides information on asymptomatic people who have unrecognized ischemic heart disease (4,5) and COPD (6,7), both killing more people than lung cancer each year.

Recognition of unsuspected diseases on imaging tests performed for different indications led to an editorial by Lee and Forman in *Radiology* (8) in 2010 regarding three articles which demonstrated that useful, but unsolicited, quantitative information could be obtained from CT scans about coronary artery calcifications (CAC) (5), bone density (9), and the size of the aorta (10). In their editorial, Lee and Forman reached the following conclusion: "*This paradigm shift allows for a rich avenue of further research and development. Rather than shying away from this new responsibility, the radiology leadership should embrace the possibility of adding a new dimension to our profession. By extracting potentially important information from existing images beyond our usual interpretation, we as radiologists can cement the three tenets that define our specialty: our mastery of technology, our clinical acumen, and our dedication to patient safety and quality.*"

Cardiovascular disease and pulmonary diseases have been identified in a significant proportion of people, being screened or being imaged for other reasons, who are unaware of their disease (4-7,11). This approach has now been incorporated in LDCT screening for lung cancer in regard to CAC; the American College of Radiology registry includes this as a required data element (12,13).

LDCT is a low-radiation dose scan without contrast injection that requires only seconds to obtain and it can be used to identify early manifestations of three of the top ten causes of death. Beyond these diseases, the LDCT provides information on other diseases of the lungs, mediastinum, breasts, bones, and upper abdomen, which may be better treated when identified early. The current vision of LDCT screening provides a comprehensive "health check" of the lungs, heart, and other organs visualized on the LDCT, particularly as LDCT radiation doses are almost as low as chest radiography (14-17). LDCT findings and follow-up recommendations have been developed over the past 20 years of LDCT screening since the initial publication on LDCT screening and long-term follow-up (18-20). There is consensus that relevant findings of these other organs are important components of the LDCT report provided to each screening participant.

A comprehensive "health check" optimal LDCT screening requires a carefully-specified, validated regimen for identification and interpretation of critical LDCT findings and the appropriate follow-up recommendations. Once developed, the recommendations have been incorporated into the International Early Lung Cancer Action Program (I-ELCAP) screening protocol (21) which has allowed for further evaluation of the usefulness of the recommendations. This vision is gaining increasing recognition throughout the world. An entire session at the 20th World Conference on Lung Cancer (WCLC) in Barcelona, Spain in September 2019 was devoted to these other findings (22).

Structured reporting of LDCT screenings and a comprehensive screening management system has allowed for the development of the recommendations. In addition, a common CT acquisition and image reconstruction protocol for both baseline and repeat screenings is important for the interpretation of the findings and change over time, particularly also for future advanced image analytics. Of course, over time, these protocols need to be updated with understanding that this can impact the interpretations.

The resulting large, well-documented database has also enabled the advancement of image analytics and statistical techniques for computer-aided diagnosis of diseases that can be identified in screening. For cardiovascular disease, automated image analysis software can measure the amount of CAC accurately, with a correlation coefficient of 0.88 compared to visual scoring (23); deep-learning approaches have also shown good performance for measuring CAC (24-26). There are also automated techniques for measuring the pulmonary artery and aorta that show good agreement with manual segmentation, with a Dice similarity coefficient of 0.933 (27). Automated image analytics have also shown promise for detecting pulmonary diseases such as emphysema (28-31), airway wall thickening (32,33), all seen in COPD (34,35), and interstitial lung disease (ILD) (36,37). In these analyses, the lung parenchyma is classified according to density and texture using machine learning and deep learning methods. An automated algorithm was able to identify early stage usual interstitial pneumonia (UIP), a form of ILD, with an area under the receiver operating characteristic curve of 0.95 (36). In addition to pulmonary and cardiovascular disease, from the same screening LDCT, automated image analytic algorithms have been used to measure breast density (38), cardiac visceral fat (39), and liver density (40). Low liver density is associated with hepatic steatosis, and the automated image analytic technique was well correlated with manual measurements by a radiologist, with an intraclass correlation coefficient of 0.94 (40). These algorithms are in various stages of development; many have been integrated into commercial systems, but often as part of separate packages that require

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extensive radiologist interaction.

In the future, as algorithms continue to improve, assessments can be made quantitatively and automatically immediately upon the LDCT screening being obtained. These would immediately be included in the radiologic report (41). Currently, however, the CT findings must be identified and measured by radiologists.

Below we briefly discuss each of the added findings that can be identified on LDCT screening for lung cancer, other than lung nodules. The protocol for lung cancer screening and identification of potential lung cancers has been extensively reported, including in our recent article (41). In this report, we focus on the key findings and recommendations for the added findings that we have developed. A summary of each of the findings and recommendations are summarized in Appendix 1. Other important findings, such as osteoporosis leading to subsequent fractures and bronchiectasis are frequent finding in participants in a screening program, and early diagnosis may avoid subsequent significant morbidities, particularly in those participants with COPD. These are being currently being addressed but are not yet completed.

The 2016 Society of Cardiovascular Computed Tomography and the Society of Thoracic Radiology (SCCT/STR) guidelines on non-contrast, non-gated chest CT scans provide a comprehensive review of the best scientific evidence and practice patterns of experts with practical recommendations based on CAC scoring methodologies, interpretation and reporting (13). The guidelines state that CAC should be evaluated and reported on all non-contrast chest CT examinations (Class I indication). They also suggested that CAC should be estimated as none, mild, moderate or severe (Class I), that it is reasonable to perform ordinal assessment of CAC which assigns a score of 0 to 12 (Class IIa) (see Appendix 1) or to perform Agatston CAC scoring (Class IIb) on all non-contrast chest CT examinations. The prognostic value of these measuring methods for cardiovascular events has been well documented.

Coronary artery calcifications (CAC)

CAC can be easily detected, measured, and reported on lung screening CT without extra radiation or cost. Reporting on CAC enhances the benefit of lung cancer screening by providing the clinicians with an additional powerful risk stratification tool that can improve the management of primary prevention of cardiovascular events particularly for the patient-clinician's discussion regarding the initiation/withhold/intensification/avoidance of statin treatment for primary cardiovascular disease prevention as CAC is well accepted as a potent CVD risk modifier.

Aortic valve calcifications (AVC)

AVC measured on electro-cardiographic-gated (ECG) CT using Agatston score, has been shown to be of prognostic importance for future CVD events, cardiovascular death, and all-cause mortality in the general population (42,43). It is of particular importance in patients with diabetes, aortic stenosis, or on hemodialysis. Meta-analyses also demonstrated the prognostic significance of AVC (44,45).

AVC on LDCT has been shown to predict death from CVD in smokers beyond that provided by CAC (46,47). LDCT scans can be used to classify AVC as none (AVC score =0), mild (AVC score =1), moderate (AVC score =2), and severe (AVC score =3) and provide recommendations for further cardiac evaluation (47) (Appendix 1). Review of a cohort of 8,618 smokers enrolled in LDCT screening for lung cancer in New York State between June 2000 and December 2005 showed that the prevalence of AVC significantly increased (P<0.0001) with the increasing severity of the Ordinal CAC scores (36). CAC and AVC were significant predictors of CVD death when considered alone using multivariable Cox regression analysis (adjusted HR of CAC =1.57, P=0.04; adjusted HR of AVC =1.39, P=0.045). For AVC>0 and CAC≥4, the hazard ratio of CVD death was 2.35 (95% CI: 1.57–3.50) compared with the reference group of AVC=0 and CAC<4, when adjusted for other risk factors. As the presence of AVC identified on LDCT is a significant predictor of future CVD death, particularly for those with ordinal CAC score ≥4, AVC scores should also be reported on screening LDCTs. For moderate and severe AVC, referral to a cardiologist is recommended and possible echocardiography as there is a high probability of aortic stenosis.

Pulmonary hypertension

Pulmonary hypertension is a progressive, potentially fatal disease, it is often difficult to diagnose early due to non-specific nature of symptoms. Pulmonary hypertension is associated with increased morbidity and death in many respiratory and cardiac disorders, and with all-cause mortality, independent of age and cardiopulmonary disease (48-53). The main pulmonary artery diameter (MPA), and

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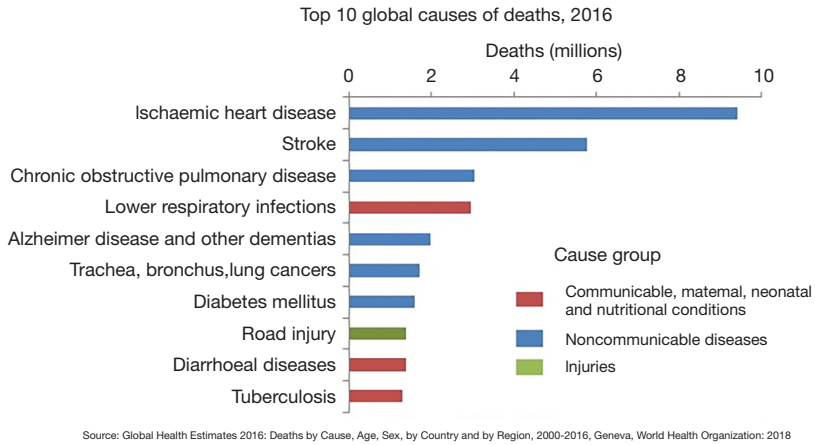

Figure 1 Most frequent causes of death.

ratio of MPA to adjacent ascending aorta (AA), MPA:AA, on Chest CT are strong indicators of suspected pulmonary hypertension.

We reviewed consecutive baseline LDCT scans of 1949 smokers in an Institutional Review Board (IRB)-approved study (54). We measured the diameter of the MPA and AA on an axial CT image at the level of the MPA bifurcation at the widest diameter vertical to its long axis and of the adjacent AA diameter by experienced chest radiologists in the smokers participating in the screening program. We determined the mean and standard deviation of the MPA and the MPA:AA ratio. Abnormally high values were defined as being more than two standard deviations above the mean which was MPA ≥34 mm and MPA:AA ≥1.0. The prevalence of MPA ≥34 mm and MPA:AA ≥1.0 was 4.2% and 6.9%, respectively. Multivariable regression demonstrated that body mass index was a significant risk factor, both for MPA ≥34 mm (OR=1.07, P<0.0001) and MPA:AA ≥1.0 (OR=1.04, P=0.003). Emphysema was significant in the univariate but not in the multivariate analysis. If pulmonary hypertension is confirmed, its natural history may be improved following targeted therapy specific for the different possible etiologies (54).

In view of the significant risk of morbidity and mortality in subjects with pulmonary hypertension, an MPA ≥34 mm or MPA:AA ≥1.0 should prompt a pulmonary consult to determine its etiology, and an evaluation of symptoms, signs, or illnesses associated with pulmonary hypertension. If it is confirmed, the natural history of pulmonary hypertension may be improved following targeted therapy specific for the different possible etiologies (54).

Pulmonary diseases

Chronic obstructive pulmonary disease (COPD)

COPD can be detected on LDCT screening for lung cancer. As shown in *Figure 1*, COPD is a leading cause of death and causes more deaths than lung cancer. COPD is characterized by chronic airflow limitation caused by a mixture of small airways disease and parenchymal destruction (emphysema) (6,7). Until CT was available, pathologic diagnosis of emphysema was made either after a lung resection or after death. Alterations in the diffusion capacity for carbon monoxide (DLCO), measured in the pulmonary function laboratory, can indicate the presence of emphysema. With the advent of computed tomography, emphysema can now be diagnosed and quantified non-invasively. In 2007, de Torres and his colleagues (6) were the first to show that the presence of emphysema on LDCT was associated with a 2.5-fold increased risk of lung cancer. Interestingly, de Torres et al showed that the presence of COPD defined by spirometric criteria (i.e., FEV1/FVC <70%) was associated with an increased risk of lung cancer in a univariate analysis, but no longer in the multivariable analysis after adjusting for the presence of emphysema while emphysema remained an independent predictor of lung cancer risk. These results have been confirmed and validated by subsequent studies which also demonstrated that emphysema and COPD are very prevalent, but underdiagnosed (11). Lung cancer screening provides an opportunity to uncover the high proportion of individuals with emphysema and abnormal airway thickening who have never been diagnosed.

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Data showed that 80% of individuals with lung cancer will have COPD, emphysema or both (6). It is very likely that the improvements in all-cause mortality observed in several randomized controlled studies (55) and the long-term survival rates observed in one-armed studies such as I-ELCAP (19) reflect in part the benefit of earlier diagnoses of COPD and/or emphysema. In other words, lung cancer screening may be the first intervention that actually improves mortality rates in patients with COPD.

Pulmonary fibrosis

Pulmonary fibrosis is scarring of the lung parenchyma. There are many types of pulmonary fibrosis but idiopathic pulmonary fibrosis (IPF) is the most common in the United States and has the worst prognosis with median survival ranging from 2 to 5 years (50,51).

IPF is a progressive fibrosis disease without known etiology affecting older men and women.

In order to make the diagnosis of IPF, a patient must have no known cause for their fibrosis and have a UIP pattern on chest CT. If the findings on chest CT are inconclusive, the patient may need a biopsy for diagnosis, which is associated with risk of fibrosis exacerbation (56-59). LDCT scans used for lung cancer screening are useful for diagnosing fibrosis.

IPF is associated with cigarette smoking and older age. Therefore, it is not surprising that when we reviewed 951 lung screening participants, that 63 (6.6%) had pulmonary fibrosis (56), much higher than reported in the general population which is 30 among 100,000 people. IPF was significantly more frequent in men (P=0.007) and associated with increasing age (P<0.0001). The most common pattern was peripheral fibrosis in multiple lobes without honeycombing. The presence of honeycombing was significantly associated with progression of fibrosis (P=0.0001) and extent (P=0.005). Early diagnosis is important as better treatments that delay progression have been developed.

A radiologist can make the confident diagnosis of UIP on high resolution CT when a patient has sub pleural basilar predominant fibrosis and honeycombing as described by the American Thoracic Society (ATS) guidelines (57). Honeycombing is defined by stacked cysts which touch the pleural surface; it typically represents advanced disease. If there is no honeycombing, then the radiologists should call it a "Probable UIP" pattern and biopsy may be necessary for confirmation of IPF. The presence of extensive mosaic attenuation, ground glass opacity, cysts and nodules suggest an alternative diagnosis (58). In the asymptomatic smoking population interstitial lung abnormalities (ILAs) will be detected. These ILAs are essentially very early fibrosis involving less than 5% of the lung parenchyma. Combined pulmonary fibrosis and emphysema is an important radiographic diagnosis with significant centrilobular type emphysema and a UIP pattern (59). Radiologists should describe these findings as they are associated with an increased risk of lung cancer and will likely progress over time (60).

Patients with fibrosis of the lung are living longer because of earlier interventions and treatment of co-morbidities. The longer patients live with fibrosis the greater is their risk for developing lung cancer. The lung cancer that occurs in the setting of pulmonary fibrosis is different from the lung cancer that occurs in emphysema as it typically occurs within the fibrosis and thus lower lobe predominant and peripheral, and the cancers are more aggressive (61).

Early findings of UIP have been classified as pre-honeycomb and honeycomb (HC) findings (56,62). Other interstitial diseases can also be identified and may differ in location and findings (62). Pre-honeycomb findings may start with traction bronchiectasis alone and then progress to ground-glass opacification and reticulations, typically at the periphery of the lungs and at the lung bases. The likelihood of disease progression is associated with honeycombing. Early identification is important for early treatment.

ILAs are minimal, incidentally identified parenchymal abnormalities on CT scan, affecting more than 5% of the lung. ILAs include traction bronchiectasis, ground-glass opacities, reticular abnormalities, and honeycombing. ILAs are associated with increased risk of developing fibrosis with its associated respiratory compromise and mortality (63). Whittaker Brown *et al.* (64) demonstrated that a significant number of smokers have ILAs and these smokers are at increased risk for lung cancer. People with ILAs should be screened for lung cancer and referred to pulmonologists for observation and/or early treatment (65).

Mediastinal abnormalities

Mediastinal abnormalities and masses

Mediastinal abnormalities and masses can occur anywhere in the mediastinum, including in the thymus, heart, and esophagus; and masses in the neck, such as the thyroid, may extend into the mediastinum (66). Such mediastinal and soft

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tissues masses are documented as to location and size. With the introduction of CT scanners, recognition of mediastinal abnormalities markedly increased, including vascular anomalies.

The frequency of mediastinal abnormalities in the context of LDCT screening for lung cancer, which focuses on older smokers, was not known. For this reason, in 2006, we published the results of our review of the LDCTs of 9,263 participants in I-ELCAP performed between 1992 and 2002 (66). We found that 71 (0.77%) had a mediastinal mass on baseline screening. Of the 71 participants with mediastinal masses, 41 were thymic masses, 16 thyroid masses, two esophageal cancers, six tracheal-esophageal diverticula, and six were masses other than those listed. Among the 11,126 annual repeat screenings, only one (0.01%) new mediastinal mass was identified (66). Of the 41 thymic masses, 5 were larger than 30 mm in diameter and all five were resected and the diagnosis was thymic carcinoma in one and noninvasive thymomas for the other four. Of the remaining 36 thymic masses, 25 had follow-up LDCT on year later; of the 25, five increased, two decreased, and 18 remained unchanged. All 16 thyroid masses were due to goiter and remained unchanged on follow-up 1 year later.

Thymic masses

Thymic masses of screening participants were reviewed (66). Based on the frequency and natural course of thymic masses identified in baseline and annual repeat screenings for lung cancer, the following work-up recommendations are made: If the mass is 3.0 cm or less in diameter on baseline CT without invasive features (e.g., irregular borders or loss of fat planes), follow-up CT 1 year later is recommended. If the thymic mass is greater than 3.0 cm or shows growth on the follow-up CT, then further workup according to standard practice is recommended.

Thyroid

Thyroid abnormalities were evaluated in 2,309 participants who had baseline and annual repeat screening at Mount Sinai Health System under an IRB approved HIPAA compliant LDCT screening program between January 2010 to December 2016. This review identified thyroid nodules in 57 (2.5%) participants on baseline screenings. Increasing age, increasing CAC score and increasing breast density grade were significant predictors for women having an incidental thyroid nodule (ITN). No significant predictors were found for men. New thyroid nodules were identified in 7 (0.15%) participants among 4,792 of annual repeat LDCTs, suggesting slow growth as it would take approximately 16.8 years of growth on average for a new thyroid nodule detected on annual rounds of screening. The American College of Radiology (ACR) provides recommendations for ITNs detected in general population (67).

Breast abnormalities

Breast density

Breast density can be easily determined on LDCT (68). It is an important risk factor for breast cancer and may also mask tumors on mammography even when digital breast tomosynthesis is used (69). More than 30 states in the United States passed mandatory density notification to patients after their mammograms so that women are better informed about their breast cancer risk and can choose to have supplemental screening with breast ultrasound or MRI. In 2019, the FDA began the process of making reporting breast density on mammography a federal requirement in both the health provider report and the patient lay letter. For women who do not have mammograms, however, LDCT may be the first and perhaps only way a woman can learn about her breast density as it cannot be determined by physical exam.

Breast density is defined in the Breast Imaging Reporting and Data System (BI-RADS) Atlas developed by the ACR (70). The four BI-RADS breast categories are: (I) almost entirely fatty; (II) scattered fibroglandular densities; (III) heterogeneously dense (which may obscure small masses), and (IV) extremely dense.

The clinically relevant differentiation is between categories A-B and C-D (68,71). If the breast tissue is, category C or D, this should be noted in the report as it suggests an increased risk for breast cancer and if clinically indicated, ultrasound (72) or MRI (73) of the breast may be considered for supplemental screening as the dense tissue might obscure an early cancer or precursor lesion on mammography.

Breast masses

Breast masses and larger breast calcifications can be seen on LDCT (74). Often these findings are known from prior breast imaging and require no work-up. Others are typically benign and also require no work-up, but if new or changing,

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a recommendation for dedicated breast imaging may be life changing. The breast findings on LDCT can be stratified into a system analogous to BI-RADS for ease of reporting and follow up (70).

Vascular calcifications seen on mammograms also provide information about coronary artery disease and should be reported (75,76). This added benefit of mammography created much interest (77). As some suggested that this information did not need to be reported, a subsequent survey (78) showed that women overwhelmingly wanted to have this information if available from mammography.

Abdominal abnormalities

Adrenal lesions

Adrenal lesions may be due to diffuse enlargement, focal nodularity, or a mass (79,80). The prevalence and natural history of adrenal lesions have been reported in many different settings. They increase with increasing age, from 0.2% of CT scans of people aged 20–29 years to 7–10% for older people (81). They are more frequently found in women, although this may be because women had abdominal imaging more frequently as no gender differences have been found in autopsy series (82). Reports suggested that 70–94% of the adrenal abnormalities are due to benign, non-secreting hyperplastic glands in asymptomatic people without history of known malignancy.

We determined the frequency of adrenal enlargement in 4,776 participants of CT screening for lung cancer at the Mount Sinai Health System who had signed HIPAA-compliant informed consents (83). We demonstrated the progression of enlargement during follow-up, separately for the baseline and annual repeat rounds. The adrenal gland was defined as enlarged when it measured 6 mm or more at its largest diameter.

On baseline screening, 202 (4%) of 4,776 participants had adrenal enlargement. Significant factors were age (OR=1.4, 95% CI: 1.2–1.7) and current smoker (OR=1.8, 95% CI: 1.3–2.4). Frequency of adrenal enlargement increased with increasing pack-years of smoking (P=0.04). Follow-up scans 7–18 months after baseline for 133 of the 200 cases with adrenal enlargement less than 40 mm showed it decreased or was unchanged in 85 (64%), and increased by less than 10 mm in 48 (36%). Five (0.04%) cases of adrenal enlargement were newly identified after baseline screening, but none increased beyond 40 mm on follow-up. Adrenal enlargement was a significant predictor of a subsequent diagnosis of lung cancer in screening (OR=2.0, 95% CI: 1.2–3.4).

We recommended that participants with adrenal enlargement of 40 mm or less in largest transverse diameter on baseline and repeat screening with low attenuation can be reasonably assessed on subsequent annual screening, based on our evaluation and that of others as described in the article (83). Suspicious imaging findings suggesting more immediate workup are: irregular borders, heterogeneity, hemorrhage, central necrosis, or calcifications. When either adrenal gland measures 40 mm or more in the largest transverse diameter, further evaluation is recommended (83).

Hepatic steatosis (HS)

HS is the most common finding in the upper abdomen in asymptomatic people. It is due to an excess accumulation of lipids in hepatocytes and can be progressive and lead to cirrhosis, liver failure, and hepatocellular carcinoma (84-86). Radiologists have an important role as this condition is frequently asymptomatic and cannot be diagnosed by any currently available blood test. It can be due to non-alcoholic and alcoholic liver diseases. Prevalence rates of 17–46% for HS have been reported in adults in Western countries (87). A single publication on follow-up liver assessment using magnetic resonance imaging reported that 13.8% of the 367 participants without known liver disease had HS (88). LDCT provides fast, reproducible, objective, and noninvasive measurements of moderate and severe HS (89-92).

Review of baseline LDCT scans of the chest of 170 participants in an IRB approved study between August 2011 and April 2016 was performed (93). The liver was divided into four sectors (left lateral, left medial, right anterior, right posterior), as defined by the Couinaud segmentation system. In each sector, a standard 1.0 cm^2 region of interest (ROI) was selected, avoiding other lesions and large blood vessel. Measurements were made using standard mediastinal window settings (width 350 HU; level 25 HU) and the average attenuation and its standard deviation were calculated. Splenic CT attenuation measurement are obtained in the same fashion. Average liver attenuation was 57.6 HU (standard deviation of 9.3) and average liver/spleen (L/S) ratio was 1.3 (SD 0.3). Liver attenuation was <40 HU for 9 (5.3%), liver/spleen (L/S) ratio <0.8 for 6 (3.5%) and either <40 HU or L/S ratio <0.8 for 9 (5.3%). Male sex (P=0.004), diabetes (P=0.0005), emphysema (P=0.03), and high BMI (P=0.0006) were significant

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predictors of HS. Aspartate aminotransferase (P=0.0018) and alanine aminotransferase (P=0.012) were negatively correlated with liver attenuation. Thus, LDCT detected HS in asymptomatic participants with frequencies similar to previous reports (94,95).

Based on the findings, if liver attenuation is below 40 HU and/or the L/S ratio below 0.8, we recommend follow-up with a primary care physician or liver specialist for further evaluation of possible hepatic steatosis detection (93,96).

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