Editorial

Utility of computed tomography lung cancer screening and the management of computed tomography screen-detected findings

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Provenance: This is an invited Editorial commissioned by Executive Editor-in-Chief Dr. Jianxing He (Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China).

Comment on: Chung M, Tam K, Wallace C, *et al.* International Early Lung Cancer Action Program: update on lung cancer screening and the management of CT screen-detected findings. AME Med J 2017;2:129.

Submitted Feb 21, 2018. Accepted for publication Feb 27, 2018.
doi: 10.21037/jtd.2018.03.68
View this article at: http://dx.doi.org/10.21037/jtd.2018.03.68

Lung cancer is one of the most common malignancies with estimated 222,500 new cases in 2017 of which approximately 20% are in non-smokers (1). Computed tomography (CT) plays a key role in lung cancer management including non-invasive *in vivo* initial diagnosis, staging and evaluation of treatment response. Since 1990s, CT of the chest has been used as a screening modality for lung cancer detection, with rates of CT utilization in lung cancer detection increasing at a rate of 10 percent annually (1). Over the past few decades, various imaging protocols and rates of interval chest CT's have been utilized in lung cancer screening programs. The variations in these protocols were in part due to integration of newer technologies ranging from development of new CT hardware and software which allowed for more precise imaging while reducing patient radiation exposure (1). The ultimate goal of these trials, as with any screening trial, was to detect lung cancer at the earliest possible stage while limiting unnecessary tests.

Recently, Chung *et al.* (1) published a comprehensive review article updating lung cancer screening and management of findings detected on screening chest CT examinations. The article shares the strength of most good review articles. For example, it provides an excellent overview of the topic at hand [international early lung cancer action program (I-ELCAP) lung cancer screening protocol], highlights key features of imaging guidelines, it's impact on U.S. Preventive Services Task Force (USPSTF) and Centers for Medicare and Medicaid Services (CMS), and provides comprehensive overview of management of findings on CT screen-detected findings. The article reviews the benefits of National Lung Screening Trial (NLST) screening of asymptomatic at risk individuals (age range, 55–80 years). Another strength of the article is that it highlights the benefit of continued surveillance of patients excluded by the CMS; especially those that have quit smoking and/or those patients suffering from medical conditions that "significantly reduce life expectancy" (1).

Furthermore, the article highlights the limitations of the NLST which combines duration of pack years and intensity of smoking a one risk factor instead of using each of the two as separate risk factors; which would allow for more optimal risk stratification. Also, USPSTF criteria do not include other key risk factors such as asbestos exposure which is known to significantly increase risk of lung cancer. Chung *et al.* highlight some of the more inclusive risk stratification models, such as the Bach model which estimates absolute risk of developing lung cancer within 10 years. Chung *et al.* also discuss the more inclusive approach to optimize risk stratification taken by the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial which incorporates several factors including gender, race, ethnicity, emphysema/chronic obstructive pulmonary disease (COPD), etc. Unlike

NLST, the latter two models incorporate a more complex models using variable more than just age and pack years of smoking. Retrospective analysis and empirical modeling studies demonstrate utilization of the inclusive risk models (PLCO) is superior to the more simpler model (NLST) with results showing a lower "number needed to screen" to prevent lung cancer related deaths. However, Chung *et al.* do not re-address these issues in the latter segments of their paper where perhaps there should be a note made on the potential impact of limited risk stratification on the strength of recommendations by I-ELCAP; something which has been accounted for by guidelines from other medical organizations.

Chung *et al.* (1) address the time and cost conundrum affecting all screening programs. They address questions related to the frequency of screening and impact of screening-associated healthcare cost. For example, Chung *et al.* discuss the effects of decreased frequency of screening from annual to biannual and how this could reduce initial cost of screening; but, this would lead to increased frequency of diagnosis of higher stage lung cancers in the screening population. This would lead to increased cost of treatment due to the higher stage lung cancer. As goal of any screening program is to maximize detection of early stage, curable lung cancers, a biannual approach would limit the efficacy of the screening program.

Chung *et al.* (1) extensively discuss the process of acquisition and interpretation of lung parenchyma and/or endobronchial nodules identified on low dose chest CT. A nodule is defined as a lesion non-linear opacity measuring less than 30 mm and is spherical shape surrounded by lung parenchyma. A lung mass is defined as nodule greater than 30 mm in size. A nodule is "classified" as non-calcified nodule (NCN) if does not meet the criteria of a benign, nodule. Key components of NCN detected on screening CT chest include: identification and characterizations of new NCNs; evaluation of known NCNs and characterization of interval change. The factors used for NCN characterization include nodule size, location, gross appearance (non-solid, part-solid, solid), nodule margins (irregular, smooth) as well as presence/absence of calcification within the nodule. Chung and colleagues provide key element of NCN that help in classifying nodules as solid, part-solid, and non-solid as this is one of the most important defining features when it comes to determining whether a NCN is neoplastic. I-ELCAP data from the past 2 decades showed no evidence of neoplasia in a non-solid NCN of size greater than 15 mm or a part-solid NCN of size greater than 31 mm (2,3). This would lead one to possible consider discontinuing interrogation of such NCNs on subsequent follow-up chest CT.

Chung *et al.* review the criteria of a 'positive' screening chest CT and what are the follow-up recommendations (1). For example, if CT appearance of the NCN is suggestive of lung cancer, histologic evaluation of nodule biopsy specimen or further evaluation for nodule metabolic activity with positron emission tomography (PET) is recommended. For metabolically active (PET positive) nodules, biopsy and histologic evaluation of the nodule is the next step in management. Metabolically inert or equivocal nodules on PET-CT should be followed up with a low-dose CT (LDCT) chest in 1 to 3 months. For concerning endobronchial nodules (e.g., solid endobronchial nodule ≥6 mm that are unchanged or increased in size on follow-up CT), follow-up evaluation with bronchoscopy is recommended. Lung nodules with biopsy did not reveal presence of lung neoplasia, follow-up with repeat LDCT in 12 months is recommended. Characteristics of concerning NCN on follow-up CT chest include: a new endobronchial solid nodule; interval growth of a pre-existing nodule or a new solid NCN of 3 to 6 mm; new nodular component of the part-solid nodule is 3 to 6 mm. Recommendation for these nodules range from follow-up PET-CT (especially if nodule ≥10 mm) or biopsy. The non-positive screening exams are considered 'semi-positive' or negative. These are recommended for continued annual repeat CT scan. Cases in which infectious and/or inflammatory process is in the differential diagnosis, e.g., patients with multiple nodules, a follow-up LDCT in 1 month is suggested to evaluate for interval change.

One of the key limitations of the this review article is its lack of comparison and contrast with the recommendations from other organizations, such as the National Comprehensive Cancer Network (NCCN) (4) and American College of Radiology (ACR) (5). Chung *et al.* noted earlier in their review the limitations of I-ELCAP and NLST. Perhaps a slightly more detailed review of the NCCN and ACR guidelines would have been helpful to the readers, especially as some of these limitations have been addressed by the NCCN and ACR guidelines (4,5). Chung *et al.*'s decision to focus on I-ELCAP is partially based on the strength of the I-ELCAP large database. Chung *et al.* do not delve into the NCCN guidelines or do the comment on the utility of the ACR's LUNG-RADs system. As part of the NCCN facility, our team incorporates key elements of the I-ELCAP, NCCN recommendations as well as utilizes

the NCN classification scheme proposed by the ACR (LUNG-RADS).

Interestingly, around the time of publication of this review by Chung and colleagues, in July 2017, the Fleischner Society Guidelines (FSG) for management of solid nodules were revised (6). FSG was initially published in 2005 by a multidisciplinary team of thoracic radiologists, pathologists, surgeons, pulmonologist, and other specialty thought leaders in lung cancer diagnosis and treatment. These new guidelines are based on evidence accumulated since the initial 2005 guidelines coupled with the experience of the leaders within the Fleischner Society. The revisions in FSG address one of the key challenges of the current LDCT for lung cancer screening—management of small subcentimeter pulmonary nodules. New FSG guidelines increase threshold size for concerning NCNs and prescribe new LDCT follow-up intervals (some of which are now given as a range rather than the previous absolute follow-up time intervals). Furthermore, the new FSG combines recommendations associated with solid and part-solid NCNs. The new FDG guidelines are more specific and simplified compared to the original FSG recommendations. An important fact to note is that FSG revision of minimum threshold size for follow-up recommendation is based on estimated NCN cancer risk of ≥1% (6). As such, guidelines proposed by the FSG would be different, if a different NCN cancer risk threshold was used.

The new FSG (6) defines low risk solitary and multiple solid NCN as those with size <6 mm for which no routine follow-up is recommended, unless patient is considered 'high risk' in which case an optional follow-up LDCT can be performed at 12 months. For low risk solitary sub solid (part-solid, ground glass) NCN <6 mm, no follow-up CT is recommended. For multiple sub solid NCN, follow-up CT at 3 to 6 months is recommended and if these are stable, then a follow-up CT in 2 and 4 years interval is recommended. For solitary or multiple solids nodules of size 6–8 mm, follow CT at 3 months is recommended or alternatively a PET-CT can be performed. For multiple ≥8 mm nodules in low and high risk patients, a follow-up CT in 3 to 6 months followed by an 18 to 24 months LDCT are recommended. Meanwhile for subsolid ≥6 mm nodules, 6 months follow-up is recommended for a ground glass nodule (with sequential follow-up every 2 until 5 years) and 3 to 6 months follow-up (with subsequent follow-ups at 1 year interval until 5 years) is recommended for the part-solid nodule. For multiple ≥6 mm subsolid nodules, follow-up CT is recommended in 3 to 6 months and subsequent management is recommended based on evolution of the "most suspicious nodule(s)". FSG incorporate LUNG-RADs classification in NCN characterization as proposed by the ACR guidelines, which further suggests the utility of the LUNG-RADs system. FSG utilized multiple risk factors including: nodule location, size, appearance, growth rate, state of lung parenchyma (emphysema, fibrosis), etc. Such an approach is what Chung *et al.* have suggested at the beginning of their review as the current best approach for risk stratification in lung cancer screenings.

In summary, Chung *et al.* review article is an excellent starting point for those new to the lung cancer screening programs as it is fairly comprehensive in providing of background of lung cancer screening. The review highlights key features of positive findings on LDCT and the recommended management options of positive and negative CT screening exams. However, for those well versed in the lung cancer screening, this review leaves advanced readers with similar questions not well addressed by I-ELCAP. For such readers, supplemental reading and understanding of the NCCN, ACR and FSG guidelines (4-6) would be of clinical and research value.

Acknowledgements

Funding: Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under award number K12CA001727 (to Ammar Chaudhry).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Chung M, Tam K, Wallace C, et al. International Early Lung Cancer Action Program: update on lung cancer screening and the management of CT screen-detected findings. AME Med J 2017;2:129.
2. Henschke CI, Yip R, Smith JP, et al. CT screening for lung cancer: part-solid nodules in baseline and annual repeat rounds. AJR Am J Roentgenol 2016;207:1176-84.
3. Yip R, Yankelevitz DF, Hu M, et al. Lung cancer deaths in the National Lung Cancer Screening Trial Attributed to Nonsolid Nodules. Radiology 2016;281:589-96.

4. Ettinger DS, Wood DE, Akerley W, et al. NCCN Guidelines Insights: Non-small cell lung cancer, version 4.2016. J Natl Compr Canc Netw 2016;14:255-64.
5. Kazerooni EA, Armstrong MR, Amorosa JK, et al. ACR CT accreditation program and the lung cancer screening program designation. J Am Coll Radiol 2015;12:38-42.
6. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology 2017;284:228-43.

Cite this article as: Chaudhry A, Gul M, Chaudhry A. Utility of computed tomography lung cancer screening and the management of computed tomography screen-detected findings. J Thorac Dis 2018;10(3):1352-1355. doi: 10.21037/jtd.2018.03.68

