Does UKLS strategy increase the yield of screen-detected lung cancers? A comparison with ITALUNG

The optimal strategy to increase the benefit of low dose computed tomograph (LDCT) screening of lung cancer in terms of as high as possible number of discovered cancers and to reduce the costs, in terms of as low as possible number of LDCT examinations and of interventions on benign lesions, is not established.

Field and co-workers recently reported[1] the results of lung cancer screening with LDCT in the UKLS RCT pilot study that selected eligible subjects with a validated individual risk prediction model, invited potential candidates by mail and applied the Wald Single Screen Design[2] with nodule management based on volumetry.[1]

We compared (table 1) some data of UKLS RCT pilot study with those of ITALUNG RCT that selected eligible subjects based on age and smoking history, invited potential candidates by mail and involved four annual LDCT screening rounds with nodule management based on diameter measurement.[3 4]

In the UKLS pilot study, higher rates of screen-detected primary lung cancers (2.1% vs 1.7%) and of stage I–II lesions (86% vs 68%) were observed. These features may be accounted for different population's characteristics including older age (mean 67 vs 61 years), higher male/female ratio (3.01 vs 1.79), higher frequency of asbestos exposure (36.0% vs 6.6%), higher prevalence of respiratory disease (52.1% vs 35.1%) and familial history for lung cancer (24.6% vs 16.8%) in UKLS screens. In particular, prevalence of lung cancer at LDCT screening can be as high as 4.2% in subjects exposed to asbestos.[5] On the other hand, the majority of the screens in UKLS were former smokers, whereas they were current smokers in ITALUNG. Twelve-month LDCT were obtained in

Table 1 Screens risk profile and results of LDCT in pilot UKLS and ITALUNG RCT

	Pilot UKLS	ITALUNG
Age (years) of selected subjects	50–75	55–69
Eligibility criteria	5-year lung cancer risk of ≥5%, based on the Liverpool Lung Project v2 risk prediction model	Smokers or former smokers of ≥20 pack/years
Sample size		
Control arm	2027	1593
Screened arm	2028	1613
Screeens' characteristics		
Mean age at randomisation (years SD)	67 (4.1)	61 (4.2)
Gender (male/female ratio)	1529/499 (3.06)	1035/578 (1.79)
Current smokers	777 (38.3%)	1060 (65.7%)
Ex-smokers	1249 (61.6%)	553 (34.3%)
Never smokers	2 (0.1%)	0
Smoking duration		
10–19 years*	117 (5.8%)	1 (0.06%)
20+ years*	1895 (93.4%)	1612 (99.94%)
Unknown*	14 (0.7%)	0
% Asbestos exposed	763 (36%)	93 (6.6%)†
% With history of respiratory disease‡	1056 (52.1%)	494 (35.1%)†
% With history of blood cancer§	26 (1.28%)	Not eligible
% With history of solid tumour¶	378 (18.6%)	Not eligible
% With family history of lung cancer	498 (24.6%)	237 (16.8%)†
% With family history of other cancer (not lung)**	1026 (50.6%)	640 (45.5%)†
Baseline LDCT completed	1994 (98.3%)	1406 (87.2%)
LDCT detected primary lung cancers	42/1994 (2.1%)	25/1406 (1.7%)††
At baseline scan	34/1994 (1.7%)	21/1406 (1.4%)
Adenocarcinoma	25/42 (59.5%)	13/25 (52.0%)
Stage I lung cancer	28/42 (66.7%)	14/25 (56.0%)
Stage I or II lung cancer	36/42 (85.7%)	17/25 (68.0%)
Surgical resection	35/42 (83.3%)	17/25 (68.0%)
Subjects undergoing 12-month scan LDCT	1015/1994 (50.9%)‡‡	1356 (96.4%)
Overall category 3 and 4 nodules§§	536/1994 (26.8%)	426/1406 (30.2%)
Of these, subjects found to have lung cancer	42/536 (7.8%)	25/426 (5.8%)
Surgical resection for benign disease	4/39 (10.3%)	1/21 (4.7%)¶¶

*All smoking (cigarettes, cigars, pipes) duration figures refer to current and ex-smokers combined.
†Information available in 1406 subjects undergoing baseline LDCT.
‡Asthma, bronchitis, TB, pneumonia, COPD or emphysema.
§Leukaemia or lymphoma, including Hodgkin's.
¶Cancers of brain, head and neck, oesophagus, breast, colon or 'other'.
††Data of ITALUNG refer to baseline and first annual repeat LDCT screening rounds.
‡‡Due to evidence at baseline of nodules >3 mm diameter.
**Cancers of brain, head and neck, oesophagus, breast, colon or 'other'.
§§Category 3 nodules correspond to: solid nodules with 5–9.9 mm diameter; part-solid nodules with non-solid component >5 mm diameter and solid component of 3–9.9 mm diameter; non-solid nodules ≥5 mm diameter.
Category 4 nodules correspond to: solid nodules ≥10 mm diameter; part-solid nodules with solid component ≥10 mm diameter.
¶¶One case of atypical adenomatous hyperplasia reclassified as adenocarcinoma in 2015.

50.9% of UKLS and 96.4% of ITALUNG screens. However, the rate of intervention for benign lesions was lower in ITALUNG (4.7% vs 10.3%).

In conclusion, the UKLS recruitment strategy increases the yield of screen-detected lung cancer compared with ITALUNG, but the gain is mild (19%). This supports the view that incorporation of additional risk factors of lung cancers as pulmonary emphysema[6] and serum biomarkers[7 8] in selection criteria of eligible subjects for LDCT screening might increase such a yield. Moreover, above data demonstrate feasibility of comparison of risk factors in subjects recruited in RCTs of lung cancer screening that is required before pooling and joint analysis of lung cancer mortality data.[9]

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