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Equations

$$x = PFN\ count\ estimate\ in\ non-lung\ cancer\ participants = \frac{(a-b+c)(1-d)e_{reader}}{f}$$

$$y = PFN\ count\ estimate\ in\ lung\ cancer\ participants = (g-h+i)(1-j)k_{reader}$$

$$Lung\ cancer\ misclassification\ rate\ estimate = \frac{y}{x+y}$$

Equation E1: NLST CT cohort lung cancer PFN misclassification rate estimate.

a = Number of eligible benign nodules = 732

b = Number of eligible benign nodules in scans which could not be processed = 3

c = Number of noncalcified solid nodules < 10 mm in the random sample of participants without lung cancer = 526

d = Post hoc benign nodule exclusion proportion = 32/246

e_{reader} = PFN proportion of benign nodules found in observer study by individual readers = 102/246 (lowest) to 185/246 (highest)

f = Proportion of randomly selected nonlung cancer participants from the population (≤ 2 mm slice thickness scans) = 5439/(26722–1089)

g = Number of eligible cancer nodules = 84

h = Number of eligible cancer nodules in scans which could not be processed = 3

i = Number of noncalcified solid lung cancer nodules < 5 mm = 13

j = Post hoc cancer exclusion proportion = 11/81

k_{reader} = Proportion of lung cancers misclassified as PFNs by individual readers = 0/70 (lowest) to 8/70 (highest)

Note.—To estimate the NLST CT cohort lung cancer misclassification rate, it was assumed that noneligible solid cancer nodules < 5 mm (n = 13) would have the same error rates and that the remaining noneligible cancers > 10 mm would never be classified as PFNs (n = 226). 26722 participants were part of the NLST CT cohort, of which 1089 were diagnosed with cancer; the random sample of participants without lung cancer considered for this study was 21% of the total CT cohort (5439/(26722–1089)). It was estimated that the proportion of cancers diagnosed among nodules classified as PFNs in the NLST CT cohort would range from 0% to 0.43%.

$$y = \text{PFN count estimate in lung cancer participants} = (g - h + i)(1 - j)k_{reader}$$

$$z = \text{Total number of nodules estimate} = \frac{l}{f} + m$$

$$\text{PFN prevalence estimate} = \frac{x + y}{z}$$

Equation E2: NLST CT cohort PFN prevalence estimate among noncalcified nodules.

a = Number of eligible benign nodules = 732

b = Number of eligible benign nodules in scans which could not be processed = 3

c = Number of noncalcified solid nodules < 5 mm in the random sample of participants without lung cancer = 526

d = Post hoc benign nodule exclusion proportion = 32/246

e_{reader} = PFN proportion of benign nodules found in observer study by individual readers = 102/246 (lowest) to 185/246 (highest)

f = Proportion of randomly selected nonlung cancer participants from the population (≤ 2 mm slice thickness scans) = 5439/(26722–1089)

g = Number of eligible cancer nodules = 84

h = Number of eligible cancer nodules in scans which could not be processed = 3

i = Number of noncalcified solid lung cancer nodules < 5 mm = 13

j = Post hoc cancer exclusion proportion = 11/81

k_{reader} = Proportion of lung cancers misclassified as PFNs by one reader = 0/70 (lowest) to 8/70 (highest)

l = Number of noncalcified nodules in the random sample of participants without lung cancer = 1796

m = Total number of cancer nodules (≤ 2 mm slice thickness scans) = 323

Note.—To estimate the NLST CT cohort prevalence of PFNs, it was assumed that the PFN proportions found in the observer study–varying from 33% (105/316) to 60% (190/316)–can be generalized to the entire sample of noncalcified solid benign nodules between 5 and 10 mm in diameter (*n* = 732) and all ineligible noncalcified solid nodules < 5 mm in diameter (*n* = 526), and that the remaining ineligible noncalcified nodules would never be classified as PFNs (*n* = 539). It was estimated that the prevalence of PFNs in the NLST would range between 24% and 44% among all noncalcified nodules.

Table E1: Summary of multicase studies with CT-pathologic correlation of intrapulmonary lymph nodes.

Study	No. subjects	No. IPLNs	Max. Diameter range	Middle/ lower lobe location (%)	Pleura attachment (%)*	Max. pleural distance (mm)*	Solid nodule (%)	Round shape (%)	Oval shape (%)	polygonal shape (%)	Sharp margins (%)	Linear densities (%)
Barnett et al, 2019 (1)	48	62	≤15‖	48 (77.4)	24 (38.7)	>10†	62 (100)	6 (9.7)	—	—	61 (98.4)	59 (95.1)¥
Kawaguchi et al, 2018 (2)	20	26	2.6 to 10.8	25 (96.2)	14 (53.8)	18	26	0 (0)	7 (26.9)	19 (73.1)	26 (100)	3 (11.5) §
Wang et al, 2013 (3)	26	31	3.4 to 9.1	30 (96.8)	25 (80.6)	8	30 (96.8)	4 (12.9)	0 (0)	27 (87.1)	31 (100)	31 (100)
Ishikawa et al, 2007 (4)	7	14	3 to 6	6 (42.9)	3 (21.4)	>15‡	13 (92.9)	1 (7.1)	2 (14.3)	11 (78.6)	13 (92.9)	11 (78.6)
Hyodo et al, 2004 (5)	10	11	3 to 9	11 (100)	3 (27.3)	12	11 (100)	3 (27.3)	0 (0)	8 (72.7)	11 (100)	9 (81.8)
Oshiro et al, 2002 (6)	16	19	5 to 12	19 (100)	10 (52.6)	8	19 (100)	9 (47.4)	10 (52.6)	0 (0)	18 (94.7)	1 (5.3)
Sykes et al, 2002 (7)	41	57	2 to 10	46 (80.7)	26 (45.6)	22	-(-)	19 (33.3)	38 (66.7)	0 (0)	—	43 (75.4)
Matsuki et al, 2001 (8)	14	18	4 to 15	18 (100)	15 (83.3)	15	-(-)	8 (44.4)	9 (50)	0 (0)	18 (100)	—
Miyake et al, 1999 (9)	4	4	9 to 10	4 (100)	1 (25.0)	3	4 (100)	3 (75.0)	1 (25.0)	0 (0)	4 (100)	—
Yokomise et al, 1998 (10)	12	12	3 to 10	11 (91.7)	9 (75.0)	5	—	—	—	—	11 (91.7)	—
Bankoff et al, 1996 (11)	17	17	4 to 12	17 (100)	0 (0)	20	17 (100)	—	—	—	—	—
Kradin et al, 1985 (12)	10	16	4 to 10	12 (75.0)	—	—	16 (100)	5 (31.3)	6 (37.5)	5 (31.3)	—	—
Pooled results	225	287	2 to 15	247 (86.1)	130 (48.0)	22	198 (99.0)	58 (22.5)	73 (28.3)	70 (27.1)	193 (98.0)	157 (71.4)

Note.—Typical CT features of IPLNs are a diameter less than 15 mm, a distance within 20 mm of the pleura, solid consistency, and sharp margins; most are located in the middle or lower lobes and display extending linear densities. IPLNs shapes can be categorized into three similarly sized groups: round, oval, or angular/polygonal. *IPLN* = intrapulmonary lymph node.

* Unspecified whether fissures were considered to be part of the pleura or not.

‖ One IPLN was excluded from the study for having a diameter ≥ 15 mm. The range was not reported; the diameters had a mean and standard deviation of 5.4 and 1.7 mm, respectively.

† 88.7% (55/62) were < 10 mm from the pleura

‡ One of 14 nodules (7.1%) was located greater than 15 mm from the pleura, but an exact distance was not reported.

¥ Described as vessels originating or terminating from the nodule. All vessels attached to IPLNs were veins; one IPLN was attached to both a vein and an artery.

§ Only linear densities continuous to the pleura were reported.

References

1. Barnett J, Pulzato I, Wilson R, Padley S, Nicholson AG, Devaraj A. Perinodular Vascularity Distinguishes Benign Intrapulmonary Lymph Nodes From Lung Cancer on Computed Tomography. J Thorac Imaging 2019;34(5):326–328.

2. Kawaguchi T, Sawabata N, Nakai T, et al. Clinical and pathological characteristics of surgically resected intrapulmonary lymph nodes: Can they be differentiated from other malignant nodules? Respir Investig 2018;56(6):473–479.

3. Wang CW, Teng YH, Huang CC, Wu YC, Chao YK, Wu CT. Intrapulmonary lymph nodes: computed tomography findings with histopathologic correlations. Clin Imaging 2013;37(3):487–492.

4. Ishikawa H, Koizumi N, Morita T, Tsuchida M, Umezu H, Sasai K. Ultrasmall intrapulmonary lymph node: usual high-resolution computed tomographic findings with histopathologic correlation. J Comput Assist Tomogr 2007;31(3):409–413.

5. Hyodo T, Kanazawa S, Dendo S, et al. Intrapulmonary lymph nodes: thin-section CT findings, pathological findings, and CT differential diagnosis from pulmonary metastatic nodules. Acta Med Okayama 2004;58(5):235–240.

6. Oshiro Y, Kusumoto M, Moriyama N, et al. Intrapulmonary lymph nodes: thin-section CT features of 19 nodules. J Comput Assist Tomogr 2002;26(4):553–557.

7. Sykes AM, Swensen SJ, Tazelaar HD, Jung SH. Computed tomography of benign intrapulmonary lymph nodes: retrospective comparison with sarcoma metastases. Mayo Clin Proc 2002;77(4):329–333.

8. Matsuki M, Noma S, Kuroda Y, Oida K, Shindo T, Kobashi Y. Thin-section CT features of intrapulmonary lymph nodes. J Comput Assist Tomogr 2001;25(5):753–756.

9. Miyake H, Yamada Y, Kawagoe T, Hori Y, Mori H, Yokoyama S. Intrapulmonary lymph nodes: CT and pathological features. Clin Radiol 1999;54(10):640–643.

10. Yokomise H, Mizuno H, Ike O, Wada H, Hitomi S, Itoh H. Importance of intrapulmonary lymph nodes in the differential diagnosis of small pulmonary nodular shadows. Chest 1998;113(3):703–706.

11. Bankoff MS, McEniff NJ, Bhadelia RA, Garcia-Moliner M, Daly BD. Prevalence of pathologically proven intrapulmonary lymph nodes and their appearance on CT. AJR Am J Roentgenol 1996;167(3):629–630.

12. Kradin RL, Spirn PW, Mark EJ. Intrapulmonary lymph nodes. Clinical, radiologic, and pathologic features. Chest 1985;87(5):662–667.