Incidental Findings on Cardiac Multidetector Row Computed Tomography Among Healthy Older Adults

Prevalence and Clinical Correlates

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Background: With the widespread use of cardiac multidetector row computed tomography (MDCT), the issue of incidental findings is receiving increasing attention. Our objectives were to evaluate the prevalence of incidental findings discovered during cardiac MDCT scanning and to identify clinical variables associated with incidental findings.

Methods: This cross-sectional analysis involved a population-based sample recruited from an integrated health care delivery system in Northern California as part of the Atherosclerotic Disease, Vascular Function and Genetic Epidemiology (ADVANCE) Study. Healthy men and women aged 60 to 69 years without diagnosed cardiovascular disease underwent cardiac MDCT for the detection and quantification of coronary artery calcification. The images were prospectively evaluated for incidental findings.

Results: A total of 459 participants underwent MDCT scanning, and the overall prevalence of any incidental finding was 41%. Of the 459 participants, 105 (23%) had at least 1 incidental finding that was recommended for clinical or radiological follow-up examination, the most common of which was single or multiple pulmonary nodules (18%). Participants with and without incidental findings had comparable baseline demographics and selected clinical variables, although there were significantly fewer men and a significantly lower prevalence of the metabolic syndrome in those with incidental findings.

Conclusions: Incidental findings, especially pulmonary nodules, are common in cardiac MDCT performed to assess coronary artery calcification in older healthy adults. The net risks and benefits of looking for noncardiac abnormalities during cardiac MDCT should be rigorously evaluated.

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INCREASED LEVELS OF CORONARY artery calcium (CAC) detected by multidetector row computed tomography (MDCT) scanning are considered a marker of atherosclerotic plaque burden and of future cardiovascular risk.[1,2] Several authors propose screening asymptomatic subjects using measures of CAC to guide the use of primary prevention therapies and improve risk stratification.[3-6] However, the discovery of noncoronary incidental findings in the course of cardiac electron beam computed tomography (EBCT) scanning has recently raised concern about population screening for CAC. Three recent studies concluded that incidental findings are a clinically important part of the assessment of cardiac computed tomographic (CT) scans and should be aggressively pursued.[7-9] On the other hand, a study of healthy active-duty Army personnel aged 40 to 45 years found that only a very small proportion of the incidental findings from EBCT screening were potentially serious.[10] Most studies of cardiac CT have enrolled selected populations and may not provide a reliable estimate of the prevalence and clinical correlates of incidental findings among healthy older individuals who are most likely to undergo screening for CAC. In addition, the results with MDCT may differ from EBCT.

To address this question, the objectives of this study were (1) to describe the prevalence and type of incidental findings discovered during cardiac MDCT scanning that were recommended for clinical or radiological follow-up examination in a sample of healthy older adults and (2) to compare baseline demographics and selected clinical characteristics in participants with and without incidental findings.

METHODS

STUDY POPULATION AND BASELINE CHARACTERISTICS

The study sample was based on the healthy older control participants in the Atherosclerotic Disease, Vascular Function and Genetic Epidemiology (ADVANCE) Study. Recruitment of these subjects has been previously described in detail.[11,12] Briefly, between December 2001 and February 2003, men and women aged 60 to 69 years were identified from the automated clinical databases of Kaiser Permanente of Northern California, a large integrated health care delivery system with more than 3 million members in the San Francisco Bay Area and surrounding counties. A random sample of persons without evidence of coronary, cerebrovascular, or peripheral arterial disease, heart failure, any systemic malignant neoplasm, significant liver or end-stage renal disease, or diagnosed dementia (using outpatient diagnoses only) were invited to participate in the study. From an initially identified sample of 84 590 eligible subjects, a cohort of 8000 persons (3608 men and 4392 women) was randomly selected as potentially eligible persons for a target recruitment goal of 1000 final enrolled participants. Letters were then sent to physicians of potentially eligible participants to confirm subject eligibility: a total of 3054 letters were sent to physicians, who eliminated 82 persons. Invitation letters were then sent to potential participants, followed by telephone screening to confirm eligibility. A total of 1390 subjects were eligible, 1063 were interested in participating, and 1023 (639 men and 385 women) were subsequently enrolled.

After obtaining informed consent, participants completed a comprehensive study visit including a self-administered health survey (including sociodemographic characteristics, medical history, and lifestyle habits), blood samples for biomarker and genetic testing, resting blood pressure, anthropometric measures, ankle brachial index, resting 12-lead electrocardiogram, brachial artery reactivity, heart rate variability, and an MDCT scan for measurement of CAC. Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria.[13,14] Physical activity was measured with the Stanford Brief Activity Survey, which categorizes activity according to metabolic equivalent tasks.[12] Institutional review boards from the Kaiser Foundation Research Institute and Stanford University approved this study.

IDENTIFICATION AND CHARACTERIZATION OF RADIOGRAPHIC INCIDENTAL FINDINGS

During the study period, CAC was assessed using 4- and 16-dectector MDCT. Initially, a Somatom Volume Zoom 4 MDCT scanner (Siemens Medical Solutions, Forchheim, Germany) was used for data acquisition. The scanning protocol acquired images with a 500-millisecond gantry rotation time, an individual detector width of 1.0 mm with a reconstructed section width of 1.3 mm, and temporal resolution of 250 milliseconds. In 2002, a Sensation 16 MDCT scanner (Siemens Medical Solutions) replaced the Volume Zoom 4 for data acquisition. All scans were electrocardiographically triggered prospectively using a sequential "step-and-shoot," nonspiral mode. Images were acquired with 16×0.75-mm-section collimation, a gantry rotation time of 420 milliseconds, tube potential of 120 kV, and an effective tube current of 500 mA. No contrast media were administered. Contiguous 3-mm-thick sections were reconstructed using half-scan interpolation from the left mainstem bronchus to the cardiac apex during peak inspiration with a 25-cm field of view. The resulting temporal resolution was 210 milliseconds at the center of rotation. The images were saved as DICOM (digital imaging and communications in medicine) files and transferred to a picture archiving and communication system. The obtained images were of the lungs (one-half to two-thirds), the superior one-third of the liver, the superior one-quarter of the spleen, the mediastinum, and the inferior one-quarter of the trachea.

Although the primary purpose of obtaining the MDCT images was to measure CAC, board-certified thoracic radiologists also read the scans for incidental noncardiac findings for the first 459 study participants. Any readings that were deemed unclear by the writing group were reread by the same radiologists for clarification. All findings requiring this second evaluation were found not to be clinically significant. For purposes of data evaluation and reporting, each finding was categorized as follows: "Location" included lung, liver, mediastinum, hilum, spleen, pericardium, heart, pleura, and other soft tissue. "Findings" were classified as a nodule, cyst, granuloma, lymph node, effusion, mass, other, and not specified. "Appearance" descriptors included ground glass, noncalcified, calcified, scar, solid, partially solid, other, and not specified. The "other" designation for appearance referred to a nonbenign appearance that was not consistent with any of the other categories. "Lesion size" was characterized as 1 to 3 mm, 4 to 5 mm, 6 to 9 mm, larger than 9 mm, multiple or scattered, and unknown or not mentioned. "Miscellaneous/other" findings included emphysema, hiatal hernia, mastectomy, heart valve, pulmonary atelectasis or inflammation, other (any other finding not otherwise categorized), and not mentioned.

For the purposes of this study, the term *pulmonary nodule* was defined as any spheroid opacity 3 cm or less in diameter in the lung parenchyma[15]; *granuloma*, as any spheroid opacity with central, laminar, or diffuse symmetrical calcification patterns; and *incidental finding*, as any finding read by the radiologist other than the CAC score. Using clinical judgment based on the best available evidence, we divided all incidental findings into "follow-up recommended" (ie, considered potentially clinically significant and recommended for clinical or radiological follow-up examination) and "no follow-up recommended" categories. In addition, for each of the reportable findings, a recommended follow-up time was assigned. For pulmonary nodules, a 1-year follow-up examination was suggested for noncalcified nodules 3 to 5 mm in size, a 6-month follow-up examination for nodules 6 to 9 mm in size, and an immediate follow-up examination for nodules larger than 9 mm. Findings other than pulmonary nodules were assigned follow-up times based on the recommendation of the primary reading radiologist. The actual clinical management of all findings was decided on by the patients and their primary physicians.

The final radiology readings were organized and coded for statistical analysis by 2 independent observers (J.R.B. and J.M.F.) in consultation with a radiologist (G.D.R.), with any disagreements adjudicated by a third observer (L.C.N.).

STATISTICAL ANALYSIS

All analyses were conducted using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina) statistical software. Continuous variables with skewed distributions were log-transformed (ie, CAC score and triglycerides). "Follow-up recommended" deemed that the participant would require further clinical or radiological evaluation. The prevalence of incidental findings was calculated. This was further subdivided into prevalence of incidental findings categorized under "follow-up recommended" and "no follow-up recommended" both by the participant and by the finding. Comparisons of different participant groups were based on unpaired *t* tests, and a 2-sided *P* value of less than .05 was considered statistically significant.

Table 1. Summary of Demographics and Selected Clinical Variables by Incidental Finding and Pulmonary Nodule Status

Variable	No Incidental Findings (n = 269)	Incidental Findings (n = 190)	*P* Value[a]	No Pulmonary Nodules (n = 372)	Pulmonary Nodules (n = 87)	*P* Value[a]
Age, mean (SD), y	65.6 (2.8)	65.3 (2.8)	.24	65.4 (2.8)	65.4 (2.8)	>.99
Men, %	52.0	42.1	.04	47.9	48.2	.95
Current smoker, %	6.3	9.5	.21	6.7	11.8	.11
Ever smoked, %	58.0	61.1	.51	58.6	62.3	.52
Diabetes mellitus, %	11.2	10.0	.69	9.6	15.3	.13
Diagnosed hypertension, %	38.3	42.6	.35	38.5	47.1	.15
Family history of cancer, %	41.6	44.7	.51	42.2	45.9	.54
Family history of coronary disease, %	46.1	45.3	.86	46.5	42.3	.49
Known dyslipidemia, %	36.8	35.8	.82	36.9	34.1	.63
Asthma, %	10.8	10.0	.79	10.2	11.8	.66
Chronic obstructive pulmonary disease, %	1.1	2.1	.39	1.6	1.2	.77
Calories from fat >35%, %	53.4	60.0	.16	55.2	60.0	.42
BMI >25, %	69.9	70.5	.88	68.4	77.6	.09
Alcohol >2 drinks/d, %	13.8	13.8	>.99	14.4	10.7	.37
Activity score >3, %[b]	14.6	12.7	.57	13.9	13.1	.84
Metabolic syndrome, %	28.4	18.6	.02	24.2	24.7	.92
C-reactive protein, mean (SD), mg/dL	2.3 (2.1)	2.4 (2.0)	.45	2.3 (2.0)	2.5 (2.2)	.67
Non–HDL-C level, mean (SD), mg/dL	154.9 (32.3)	152.5 (35.0)	.46	155.3 (33.7)	147.7 (34.3)	.06

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL-C, high-density lipoprotein cholesterol.
SI conversion factor: To convert HDL-C to millimoles per liter, multiply by 0.0259.
[a] Unpaired *t* test for means; χ^2 test for proportions.
[b] Activity instrument that categorizes activity according to metabolic equivalent tasks (a score >3 indicates moderate activity or greater).

RESULTS

The 459 participants had a mean age of 65 years and 52% were women. The overall prevalence of any incidental finding in this group of healthy older individuals was 41% (190 of 459); 105 participants (23%) had at least 1 incidental finding recommended for follow-up examination. Of the 190 participants with an incidental finding, 105 (55%) had a single finding, while the remaining 85 (45%) had 2 or more findings. A total of 307 individual incidental findings were reported, of which 148 (48%) were classified as needing clinical or radiological follow-up examination.

As given in **Table 1**, participants with and without incidental findings had comparable baseline demographics and selected clinical variables, although there were significantly fewer men and a significantly lower prevalence of the metabolic syndrome in those with incidental findings. An analysis comparing only those with pulmonary nodules vs those without also showed the 2 groups to be similar, with only a nonsignificant trend toward increased prevalence of pulmonary nodules in current smokers.

With "person" as the unit of analysis, the most common locations of incidental findings were lung (31%), liver (6%), heart (5%), hilum and "other" (4% each), mediastinum (3%), and spleen (1%) (**Table 2**). It should be noted that the sum of the organ-specific prevalences exceeds 41% because some individuals had findings in more than 1 organ. Of the patients with lung incidental findings, 59% were recommended for radiological or clinical follow-up examination. The most common incidental finding recommended for follow-up examination was the noncalcified solid pulmonary nodule greater than 2 mm in diameter, which occurred in 15% of participants. Other incidental findings recommended for follow-up included liver masses (n=3), pericardial effusions (n=14), ground glass (n=9) or partially solid (n=2) pulmonary nodules, noncalcified hilar lymph nodes larger than 1 cm in diameter (n=1), and a noncystic anterior mediastinal mass (n=1).

Almost all the lung findings (141 of 144 [98%]) were in the parenchyma or bronchi (**Table 3**). Moreover, of the 141 participants with parenchymal findings, 130 (92%) had 1 or more pulmonary nodules, of which more than half (81 [57%]) were recommended for follow-up examination. Nodules categorized as "follow-up recommended" included solid, partially solid, ground glass, spiculated, or "other" radiographic appearance. A total of 8 participants (2%) had pulmonary nodules that were larger than 9 mm (**Table 4**). The majority of participants with clinically significant pulmonary nodules had a solid nodule (70 of 81 [86%]). The most common incidental finding in participants without a follow-up–recommended finding was a pulmonary granuloma (35 of 59 [59%]). Other clinically insignificant pulmonary findings included scarring, atelectasis, pleural plaque, emphysema, and bronchiectasis. Analyzing all 459 participants (those with and without a follow-up recommended finding), 13 (3%) had incidental inflammatory infiltrates and 19 (4%) had incidentally diagnosed emphysema. Only 1 participant had incidentally diagnosed bronchiectasis.

The most common hepatic findings were benign-appearing cysts (21 of 459 [5%]). One fluid-filled mass and 3 solid liver masses were noted that required follow-up examination. Notable findings included a 41-mm noncystic, noncalcified liver mass in an asymptomatic 61-year-old woman and a 17×7-cm fluid-filled mass partially imaged in the liver of a 63-year-old woman (**Figure**).

Within the mediastinum and hilum, 29 of the 459 participants (6%) had enlarged, calcified lymph nodes. The only findings recommended for follow-up examination were a 22×12-mm noncystic anterior mediastinal mass and a 36×21-mm noncalcified hilar lymph node with enlarged adjacent lymph nodes.

The most common noncoronary cardiac incidental finding was a pericardial effusion (14 of 459 [3%]). Other clinically insignificant findings included valve calcification, pericardial cysts, and pericardial thickening.

COMMENT

In this population-based sample of relatively healthy older men and women, a surprisingly large proportion (41%) had incidental findings on cardiac MDCT. It is remarkable that in 23% of participants the incidental finding was considered notable enough to require further clinical evaluation or follow-up radiological imaging.

Four published studies have reported on the prevalence of incidental findings on EBCT screening for CAC (**Table 5**). Compared with the other study populations, our sample was generally older, with fewer men and a larger proportion of current or former smokers. In addition, our study included data obtained from MDCT, whereas the other studies evaluated data obtained from EBCT. While EBCT and MDCT have been recently compared for CAC scoring, no study to date has contrasted the ability of EBCT vs MDCT to detect incidental findings.[18] The improved spatial resolution of MDCT compared with EBCT might explain the higher rate of pulmonary nodules in our study compared with the studies using EBCT.

In our sample, we observed a prevalence of 18% for pulmonary nodules recommended for follow-up examination. The most common incidental finding recommended for follow-up in our sample was the noncalcified solid pulmonary nodule. A 2005 observational study

Table 2. Prevalence of Incidental Findings by Organ, With "Person" as the Unit of Analysis

Findings by Organ	Absolute No. of Patients With Incidental Findings (%) (N=459): Total Incidental Findings	Findings Recommended for Follow-up
Lung	144 (31.4)	85 (18.5)
Parenchyma/bronchi	141 (30.7)	85 (18.5)
Pleura	3 (0.6)	0
Heart	24 (5.2)	14 (3.1)
Pericardium	18 (3.9)	14 (3.1)
Cardiac valves	6 (1.3)	0
Mediastinum	13 (2.8)	1 (0.2)
Lymph node	12 (2.6)	0
Mass	1 (0.2)	1 (0.2)
Hilum	18 (3.9)	1 (0.2)
Lymph node	18 (3.9)	1 (0.2)
Noncalcified	1 (0.2)	1 (0.2)
Calcified	17 (3.7)	0
Abdomen	30 (6.5)	4 (0.9)
Liver	27 (5.9)	4 (0.9)
Mass	3 (0.6)	3 (0.6)
Fluid attenuation	1 (0.2)	1 (0.2)
Cyst	21 (4.6)	0
Granuloma	2 (0.4)	0
Spleen	3 (0.7)	0
Other	16 (3.5)	0
Hiatal hernia	9 (2.0)	0
Breast	2 (0.4)	0
Other soft tissue	5 (1.1)	0
Total	190 (41.4)[a]	105 (22.9)[a]

[a] Some patients had more than 1 incidental finding.

Table 3. Numerical Summary of Incidental Pulmonary Findings, With "Person" as the Unit of Analysis

Incidental Findings	Absolute No. of Patients[a]	Prevalence Within Study Sample, %[b]
Follow-up recommended	85	18.5
Pulmonary nodules	81	17.6
Solid	70	15.2
Part solid	2	0.4
Ground glass	9	2.0
Spiculated	1	0.2
Other (nonbenign pattern)	2	0.4
Other (nonbenign finding)	4	0.9
No follow-up recommended	59	12.8
Pulmonary nodules (granulomata)	35	7.6
Scarring/atelectasis	11	2.4
Pleural plaque(s)	3	0.6
Inflammatory infiltrate[c]	5	1.1
Emphysema[c]	8	1.7
Total participants with lung incidental findings	144	31.4

[a] Many participants had more than 1 incidental finding.
[b] Denominator, N=459.
[c] Only includes participants with these findings and no recommended follow-up examination; if study participants with recommended follow-up examination were to be included, 13 and 19 participants, had inflammatory infiltrates and emphysema, respectively.

Table 4. Summary of Pulmonary Nodules Recommended for Follow-up Examination by Type and Size[a]

Type of Pulmonary Nodule	Pulmonary Nodule Size, mm: 4-5	6-9	>9	Multiple Nodules	Size Unknown or Not Mentioned
Solid	29 (6.3)	28 (6.1)	3 (0.6)	7 (1.5)	3 (0.6)
Part solid	1 (0.2)	1 (0.2)	0	0	0
Ground glass	0	1 (0.2)	5 (1.1)	0	3 (0.6)
Spiculated	1 (0.2)	0	0	0	0
Other (nonbenign pattern)	2 (0.4)	0	0	0	0
Total	**33 (7.1)**	**30 (6.5)**	**8 (1.7)**	**7 (1.5)**	**6 (1.2)**

[a] Data are given as absolute number of patients with incidental findings (% prevalence in cohort); denominator, N=459.

in a sample of 414 otherwise healthy participants with a mean age of 65.6 years reported that none of the noncalcified nodules smaller than 5 mm found on CT had any growth over 12 months.[19] The Fleischner Society recently published criteria for evaluating noncalcified pulmonary nodules detected on nonscreening CT scans.[20] According to these recommendations, nearly 60% (noncalcified nodules larger than 4 mm) of our sample's noncalcified pulmonary nodules would require further evaluation and/or follow-up examination with radiologic imaging. No randomized controlled studies to support clinical decision making in this situation are currently available.

The 1999 Early Lung Cancer Action Program (ELCAP) described 23% of its high-risk participants (all current or former smokers ≥60 years old) who had pulmonary nodules with a nonbenign pattern at baseline.[17] The 2005 Italung-CT pilot study reported a 33% prevalence of indeterminate nodules (defined as "not completely calcific nodules or calcifications without a benign pattern") in their cohort of asymptomatic heavy smokers.[16] While these lung cancer screening studies are substantially different from the present study in both design and objective, the prevalence of pulmonary nodules was similar across studies (Table 5).

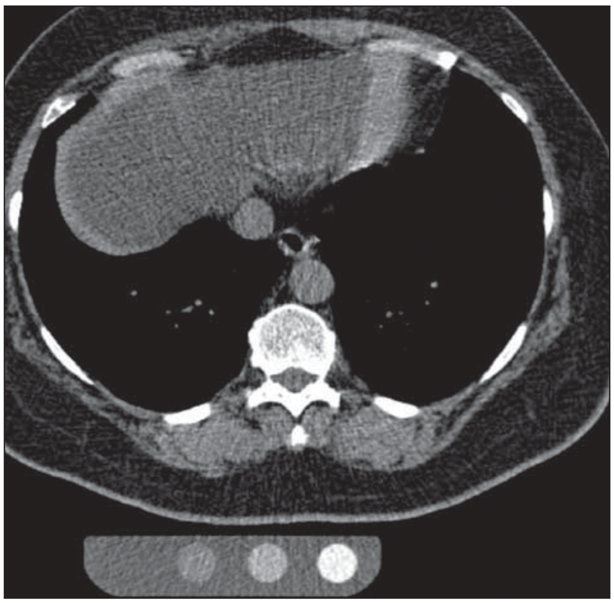

Figure. An axial multidetector row computed tomographic scan showing a 17×7-cm fluid-filled mass partially imaged in the liver of an asymptomatic 63-year-old woman undergoing quantification of coronary artery calcification.

Participants with an incidental finding on cardiac MDCT were less likely to be men or to have the metabolic syndrome. These were unexpected findings that require further investigation. We found no significant differences in selected characteristics between participants with or without pulmonary nodules, including current tobacco use, but our study may have been underpowered to detect potentially relevant associations with this and other baseline characteristics.

Limitations in our study include the relatively modest number of participants and our use of 2 different MDCT scanners (4- and 16-detector CT scanners) during the study period, although the section thickness, reconstruction intervals, and scan range were the same between the 2 scanners. We recruited participants from a health care delivery system in northern California, so our results may not be completely generalizable to other populations or health care settings. However, this limitation is somewhat mitigated by the fact that the Northern California Kaiser Permanente membership is generally representative of the larger population of the San Francisco Bay Area, with the exception of the extremes of the socioeconomic spectrum.[21]

In conclusion, the prevalence of incidental findings was high on cardiac MDCT scanning for CAC in this sample of healthy subjects aged 60 to 69 years. Nearly one-quarter of these incidental findings was considered notable enough that, according to current guidelines, additional evaluation and radiologic follow-up examination was required. With the advent of even more sensitive 64- and 128-detector cardiac MDCT scanners for CAC and noninvasive coronary angiography, it is likely that the prevalence of detected incidental findings will only

Table 5. Comparison of Incidental Findings Studies and Lung Cancer Primary Prevention Screening Studies

Incidental Findings Study	Baseline Characteristics[a]	Overall Incidental Finding Prevalence, %	Prevalence of Incidental Findings Recommended for Follow-up Examination, %[b]	Prevalence of Pulmonary Nodules Recommended for Follow-up Examination, %[c]	Noncoronary Cardiac Incidental Finding Prevalence, %
ADVANCE Study (present study)	Mean age, 65 y; men, 48%; smokers, 59%	41	23	18	5
Schragin et al,[9] 2004	Mean age, 53 y; men, 68%; smokers, 43%	20.5	4.2	3.4	NR
Elgin et al,[10] 2002	Mean age, 42 y; men, 82%; smokers, 13%	8	4.7	NR	1.2
Horton et al,[8] 2002	Mean age, 55 y; men, 64%; smokers, 25%	7.8	2.2	5	NR
Hunold et al,[7] 2001	Mean age, 59 y; men, 78%; smokers, NR	53	11	1.1	32
Pulmonary nodule studies					
Picozzi et al,[16] 2005	Mean age, 64 y; men, 78%; smokers, 100%	NR	NR	33	NR
Henschke et al,[17] 1999	Mean age, 67 y; men, 54%; smokers, 100%	NR	NR	23	NR

Abbreviations: ADVANCE, Atherosclerotic Disease, Vascular Function, and Genetic Epidemiology; NR, not reported.
[a] All except Elgin et al[10] reported both active or former smokers; Elgin et al[10] report only active smokers.
[b] Defined as any finding requiring further clinical or radiological follow-up examination.
[c] Defined as any noncalcified lung nodule larger than 3 mm requiring further investigation or follow-up examination.

increase over time. Some argue that reading and evaluating cardiac CT for incidental findings is required by physicians under the code of beneficence, while others argue that the principle of *primum non nocere* should temper attempts to identify radiologically detectable incidental findings. Our study highlights the importance of resolving these issues and the need for further data on the potential benefits, harms, and costs of searching for incidental findings during cardiac MDCT.

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