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Incidental Pulmonary Nodules in Emergent Coronary CT Angiography for Suspected Acute Coronary Syndrome: Impact of Revised 2017 Fleischner Society Guidelines

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Abstract

Background—Pulmonary nodules (PN) are frequently detected incidentally during coronary computed tomography angiography (CTA). We evaluated whether the 2017 Fleischner Society guidelines may result in a decrease of follow-up testing of incidental PN as compared to prior guidelines in patients undergoing coronary CTA.

Methods—We conducted a retrospective study of a registry of emergency department patients who underwent coronary CTA for acute coronary syndrome assessment between 2012 and 2017. Based on guidelines, patients <35 years, history of cancer, or prior exams showing stability of PN were excluded. Patients >60 years, history of smoking, irregular/spiculated PN morphology, or PN size >20mm were classified as high-risk for lung cancer. Radiological findings pertaining to PN were identified (PN size, morphology, quantity) through review of radiology reports. PN follow-up recommendations were established using 2017 Fleischner Society Guidelines and compared with prior guidelines for solid (2005) and subsolid (2013) PN. Data were analyzed with Student's t-test.

Results—The registry included 2,066 patients (female 45.1%, 52.9±11.0 years), of which 578 (28.0%) reported PN. 438 of those (21.2%) were eligible for guideline-based follow-up evaluation. 205 (46.8%) were classified as high-risk for lung cancer. 2017 guidelines reduced the number of

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Conflict of interest:

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individuals requiring follow-up by 64.5%, from 264 (12.8%) to 94 patients (4.5%) when compared to prior guidelines ($p < 0.001$). The minimum number of follow-up chest CTs decreased by 55.8% from 430 to 190 ($p < 0.001$).

Conclusion—Application of the 2017 Fleischner Society Guidelines resulted in a significant decrease of follow-up testing for incidental PN in patients undergoing coronary CTA for suspected acute coronary syndrome.

Keywords

Pulmonary nodule; lung nodule; coronary computed tomography angiography; Fleischner Society Guidelines; Management of Incidental lung nodules; incidental findings; follow-up CT; acute coronary syndrome

Introduction

Coronary computed tomography angiography (CTA) has become an alternative to functional testing for patients presenting to the emergency department with acute chest pain and low to intermediate risk for acute coronary syndrome (ACS)¹⁻³. Coronary CTA datasets not only provide visualization of cardiac anatomy, but also non-cardiac anatomy including the lower parts of the lungs below the level of carina, mediastinum, bones, and the upper parts of the abdomen⁴. Thus, extra-cardiac incidental findings are common⁵⁻¹¹, the majority being pulmonary nodules (PN) with a prevalence of 16-23%^{12, 13}. Those extra-cardiac findings result in a substantial number of additional downstream tests, especially follow-up chest CTs.

Recommendations for follow-up of solid PN were widely standardized by the 2005 Fleischner Society Guidelines for the management of incidental lung nodules and later for subsolid PN by additional 2013 guidelines^{14, 15}. Guideline-based PN follow-up substantially increases costs in patients with CTA-based, anatomic testing of acute and chronic chest pain, but has shown to result in only a minimal reduction in mortality from lung cancer and is only cost-effective in smokers, but not in non-smokers^{5, 8, 12, 16}.

In 2017, the Fleischner Society updated their guidelines recommending follow-up testing in patients with an estimated risk for lung cancer of 1% or greater¹⁷. Calculation of lung cancer risk was determined by PN characteristics such as size, location, and morphology, but also by clinical risk factors such as age, smoking history, and exposure to toxic substances. The highest impact on the number of patients with follow-up recommendations might be the increased threshold for solid PN follow-ups from 5 mm (2005 guidelines) to 6mm in the 2017 guidelines, below which a follow-up is not recommended. Also, while all patients with high risk for lung cancer received recommendations for follow-up chest CT per 2005 guidelines, patients with high risk for lung cancer, but solid PN <6 mm would not get follow-up per 2017 guidelines.

The aim of our study was to compare the number of patients with need for follow-up testing per revised 2017 Fleischner Society Guidelines for management of incidental PN versus the relevant prior applicable guidelines (2005 guidelines for solid PN, and 2013 guidelines for

subsolid PN) in patients with acute chest pain who underwent coronary CTA for ACS assessment.

Materials and Methods

Subjects

This retrospective, IRB-approved and HIPPA-compliant study was conducted using a prospectively acquired registry which included 2,066 emergency department patients (52.9 ± 11.0 years; 45.1% female), who underwent coronary CTA for ACS assessment in a tertiary, academic hospital from 2012 to 2017. The registry's inclusion criteria for ACS assessment by coronary CTA were summarized previously¹⁸, in a manuscript that dealt with the efficiency and safety of implementation of coronary CTA in the emergency department, but not related to incidental findings (and reporting only 1,022 of 2,066 patients included in the present study)¹⁸.

Coronary CT angiography

All coronary CTA scans were performed on second- and third-generation dual-source CT scanners (Siemens Somatom Flash and Siemens Somatom Force, Siemens Healthineers, Forchheim, Germany) and described in above mentioned manuscript¹⁸. Based on the scout, the scan length was set from the carina to the diaphragm covering the heart, but not the entire lungs or was tailored based on the Calcium scan images. To visualize the lungs, an image series with a maximum field of view covering the lungs over the entire scan length were reconstructed with 1.5 mm slice thickness in addition to image series with a field of view tailored to the heart. Image quality (but not incidental findings) between second- and third-generation dual-source CT scanners was reported in a subset of 246 patients¹⁹.

Pulmonary nodule assessment

PN evaluation was mandatory as part of the structured coronary CTA report and confirmed by two board-certified radiologists specialized on cardiac imaging. PN were measured in long and short axis and an averaged diameter rounded to the nearest millimeter was noted in the report (Figure 1). All radiology reports were extracted from our Research Electronic Data Capture (RedCap, Harvard Catalyst, Boston, Massachusetts) and further evaluated using Microsoft Excel (Microsoft Corporation, Redmond, Washington). Reports were screened for PN evaluation by a cardiac imaging fellow (J.S.). In cases where the radiology report did not clearly describe PN characteristics (type, morphology, size, quantity), images were reviewed by a board-certified radiologist using dedicated picture archiving and communication system (PACS) software (AGFA Impax 6.6.1.3004, AGFA, Mortsel, Belgium).

Management of incidental PN followed the 2017 published guidelines of the Fleischner Society¹⁷. Patients under 35 years or with a history of cancer were excluded, as these patients would benefit from a case-by-case based follow-up recommendation¹⁷. Patients with existing prior chest CT confirming stability (and thus no need for additional follow-up) or findings of granuloma or hamartoma were not included for further evaluation. Patients were divided into subgroups based on the amount of PN (single vs. multiple), type (solid vs.

subsolid (subdivided into pure groundglass or partly PN), size, and risk for lung cancer. As the registry only included classification of smokers into former and current smokers, further risk stratification of former smokers depending on the time since quitting could not be evaluated. Thus, all patients with a history of smoking were classified as high risk for lung cancer. Never-smokers were classified as low risk for lung cancer. Further, patients over 60 years, irregular/spiculated nodule, or nodule size >20mm were classified as high risk for lung cancer¹⁷. To allow a comparison of prior guidelines from 2005 and 2013 with the current guidelines, all solid PN were subdivided based on their size into groups of < 4 mm, 4-5 mm, 6-8 mm, and > 8 mm, single subsolid PN into < 5 mm, 5-6 mm, and > 6 mm, and multiple subsolid PN into < 6 mm and > 6 mm. Follow-up recommendations were compared between 2017 Fleischner Society Guidelines and previous versions which were from 2005 for solid PN and from 2013 for subsolid PN (Table 2)^{14, 15, 17} which were bases for our previous or current hospital's internal guidelines. Cases that did not require PN follow-up, but with a comment for optional follow-up (in 12 month) were counted as no need for follow-up. Minimal number of recommended follow-up chest CT per current (2017) and prior (2005, 2013) guidelines were calculated.

Additionally, number of recommended PN follow-ups were categorized into coronary artery disease (CAD) severity (no CAD, non-obstructive CAD, obstructive CAD) recorded within the registry using Coronary Artery Disease - Reporting and Data System (CAD-RADS,)²⁰. No CAD included patients with a CAD-RADS 0 (no plaque nor stenosis) classification. Non-obstructive CAD included CAD-RADS 1 (1-24%/minimal stenosis), 2 (25-49%/mild stenosis), and 3 (50-69%/moderate stenosis). Obstructive CAD included CAD-RADS 4A (70-99%/severe stenosis), 4B (>50% in left main coronary artery or obstructive (70-99%) 3-vessel disease), and 5 (100%/occlusion). Scans with at least one non-evaluable coronary segment, and no other obstructive CAD were classified as CAD-RADS N (non-diagnostic).

Additional extra-cardiac findings—Further incidental extra-cardiac findings (in addition to PN) were noted. In case of reported, suspected malignancy or pulmonary inflammation, patient's electronic health record was screened to confirm diagnoses.

Statistical analysis

Continuous variables were shown as mean \pm standard deviation. Groups were compared with Student's t-test for independent samples. In the case of non-normally distributed variables, median (P25-P75) were reported, and Mann-Whitney U test was used for comparison. Categorical variables were expressed as frequencies and percentages; differences were assessed using the chi-square test. Recommended follow-ups were patient-based and displayed as total numbers and percentage. P-values were two-sided, and a P-value of less than 0.05 was considered statistically significant. Data were analyzed with dedicated software (IBM SPSS Statistics v.19, IBM, Armonk, New York).

Results

PN were reported in 578 (28.0%) of the 2,066 patients included in the registry. Per guidelines, individual follow-up strategies were recommended in 22 patients with a history of cancer and in 18 patients younger than 35 years and, thus, excluded from guideline-based

PN follow-up evaluation. Further, patients with previous CT examinations confirming stability (n=70) and patients with a reported calcified granuloma or hamartoma (n=29) were excluded from guideline-based follow-up evaluation (Figure 2). In total, 438 (21.2%) patients (54.5 ± 11.0 years; 43.4% female) had incidental PN with need for guideline-based PN follow-up evaluation (Table 1).

Pulmonary nodule assessment

Of the 438 patients with need for guidelines-applicable PN evaluation, 94 (21.5%) would receive recommendations for follow-up of incidental PN per 2017 guidelines compared to 264 (60.3%) per prior (2005 and 2013) guidelines, which resulted in a significant reduction of 64.5% ($p<0.001$) (Figure 3, Table 2). Thus, only 4.5% of all patients undergoing emergent coronary CTA would receive PN follow-up testing per 2017 guidelines versus 12.8% per prior guidelines. The minimal number of follow-up chest CTs would decrease from 430 per 2005/2013 guidelines to 190 per 2017 guidelines; a reduction of 55.8% ($p<0.001$).

High risk criteria for lung cancer were noted in 205 (46.8%) of the 438 patients: age over 60 years (n=108), smoking history (n=123), PN in the upper lobe (n=100), PN size > 20mm (n=1), and irregular/spiculated PN morphology (n=1). 233 (53.2%) were classified low risk for lung cancer. Per prior guidelines (2005 and 2013), almost all patients classified as high risk for lung cancer (201/205; 98.0%) would have received recommendation for follow-up testing compared to only 55 (26.8%) patients per 2017 guidelines; a reduction of 72.8% (Figure 4, Table 2).

Evaluation of PN characteristics revealed 398 (90.9%) patients with solid PN, of who the majority (n=334) had solid PN smaller 6 mm which did not require follow-up testing per 2017 guidelines. Number of patients with PN, guideline-based recommendation for PN follow-up, and changes between the old and new guidelines are listed in Table 2 with breakdown into PN characteristics.

Coronary CT angiography

Coronary CTA ruled out obstructive CAD in most patients (n=1771; 85.7%) in that registry; the majority with no need for additional testing. 241 of those (13.6%) patients would receive recommendation for PN follow-up testing per 2005/2013 guidelines. Application of the 2017 guidelines, only 88 (5.0%) patients without obstructive CAD would receive recommendation for PN follow-ups, a reduction of 63.5% ($p<0.001$) (Figure 3, Table 3). Similar, the minimum number of follow-up chest CTs in patients without obstructive CAD would decrease by 55.9% from 392 to 173 follow-up chest CT scans ($p<0.001$). In all CAD categories (no CAD, non-obstructive CAD, obstructive CAD), the number of patients with need for PN follow-up testing and the minimal number of follow-up chest CTs would be significantly lower applying the revised 2017 guidelines instead prior (2005, 2013) guidelines (Table 3).

Additional extra-cardiac findings—Incidentally detected malignancies were reported and clinically confirmed in 2 patients (0.1%) (Esophageal cancer, n=1; Cholangiocarcinoma, n=1) Further extra-cardiac findings are listed in Table 4.

Discussion

A rate of 28% incidental PN in coronary CTA is in accordance with prior studies^{6, 7, 9}. Our results showed that the 2017 Fleischner Society Guidelines for the management of incidental PN could lower the number of follow-up recommendations by 64.5% compared to prior, 2005 and 2013, guidelines in coronary CTA patients. Thus, the revised guidelines would decrease recommendation for follow-up testing of incidental PN from 12.8 to 4.5% of all patients presenting to the emergency department with acute chest pain and low to intermediate risk for CAD whom underwent coronary CTA for ACS assessment.

Revised 2017 Fleischner Society Guidelines did not recommend follow-up testing of single or multiple solid PN <6mm in both nonsmokers and smokers, which represented the majority (76%) of our cohort^{17, 21–24}. In comparison, 2005 guidelines for solid PN did not recommend follow-up only in low-lung-cancer-risk patients with solid PN ≥ 4 mm. Thus, 72.3% less follow-up testing of solid PN would be recommended per 2017 guidelines to 2005. Due to the relatively few patients with single subsolid PN <6 mm, the impact of a higher diameter threshold value of <6 mm (2017 guidelines) instead <5 mm (2013) for follow-up testing did only result in a reduction of 11.8% follow-up testing recommendations. There is no change in the follow-up recommendations in patients with multiple subsolid PN, independent of the PN size. Suspicious morphology, upper lobe location, or both, increase cancer risk to 1-5% and, thus, follow-up chest CT “may be considered”¹⁷. As coronary CTA only covers the lower lung zones, potential lung cancers in the apices might be missed. However, imaging of the entire lungs within emergent coronary CTA without clinical necessity is ethically problematic and not encouraged by the 2017 Fleischner Society Guidelines themselves¹⁷.

The number of patients actually completing the recommended follow-up care is substantially lower than the number of recommendations^{25, 26}. Addition of the Fleischner Society Guidelines within the radiology report has shown to significantly increase the likelihood of undergoing recommended follow-up care²⁵. In combination with the significantly lower number of follow-up recommendations per 2017 guidelines, we speculate that the likelihood of completing recommended follow-up care may increase. The substantial reduction of recommended PN follow-up testing in patients with ruled out CAD per CTA might also increase the acceptability of coronary CTA, which has been proven to be an excellent non-invasive alternative to rule out CAD/ACS compared to standard care^{1, 3}, but has not been widely accepted²⁷. Although extra-cardiac findings are common, clinically significant incidental findings are less prevalent. Nevertheless, 2 of our patients had incidentally detected extra-cardiac malignancies which would have been missed by functional testing for CAD assessment. To keep the number of missed extra-cardiac findings low, we propose that readings should be performed by imagers familiar with cardiac CT; this becomes more important as the technology diffuses, appropriate indications widen, and CTA volume increases²⁸.

There are several limitations that require acknowledgment. First, our experience is based on a single-center registry of a tertiary urban academic hospital. Second, the retrospective design of our study did not allow evaluation of the actual follow-through and performance of

recommended follow-up chest CTs^{29, 30}. Our study focused on the expected amount of recommended follow-up testing comparing prior and revised Fleischner Society Guidelines. Further, not all risk factors for lung cancer could be determined based on the registry data (for example, date of smoking cessation, which might downgrade cancer risk). Third, coronary CTA does not cover the entire lungs which might underestimate nodule burden, and thus lung cancer risk in this cohort (this point is the basis of a work focusing on coronary CTA applicability of nodule follow-up guidelines, as opposed to whole-chest CTA).

In conclusion, management of incidental PN as per 2017 Fleischner Society Guidelines would reduce the number of recommended follow-up testing by 64.5% from 12.8 to 4.5% in patients undergoing coronary CTA compared to prior guidelines. This will lower cost for follow-up testing of incidental findings in coronary CTA, and may increase the acceptability of coronary CTA.

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Abbreviations

ACS	acute coronary syndrome
CAD	coronary artery disease
CAD-RADS	Coronary Artery Disease - Reporting and Data System
CTA	computed tomography angiography
PN	pulmonary nodule

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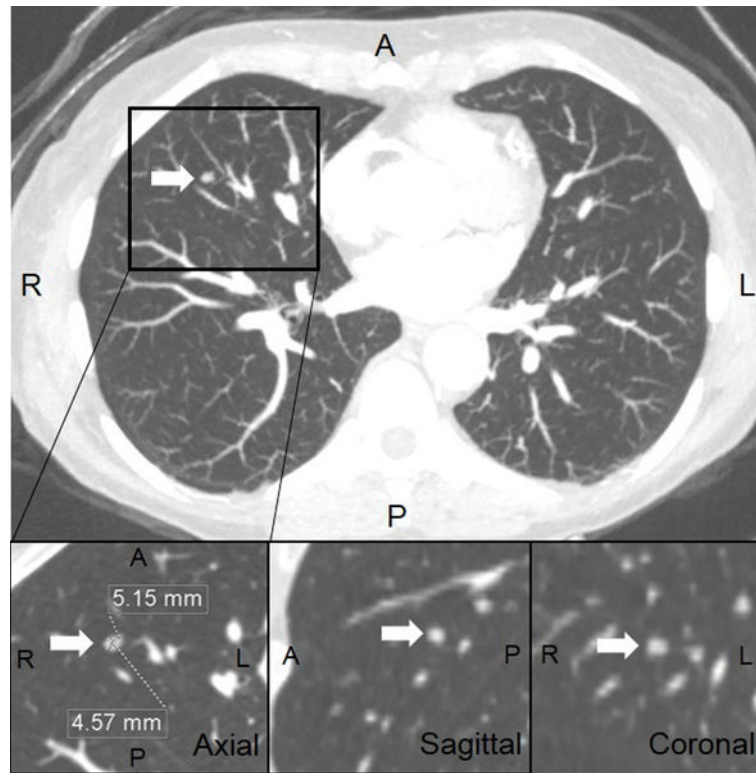


Fig 1. 62-year-old female presented with acute chest pain to the emergency department. Coronary CT angiography ruled out coronary artery disease. Reconstructed maximum field-of-view axial 3-mm-thick maximum intensity projection (MIP) images revealed a single 5-mm solid pulmonary nodule in the middle lobe (top image). Average of long and short axes were measured in 1.5 mm multiplanar reformations (MPR) and rounded to the nearest millimeter (bottom images). She was considered low-risk for lung cancer and therefore needed no follow-up chest CT per 2017 guidelines. Prior guidelines from 2005 would have recommended follow-up chest CT at 12 months.

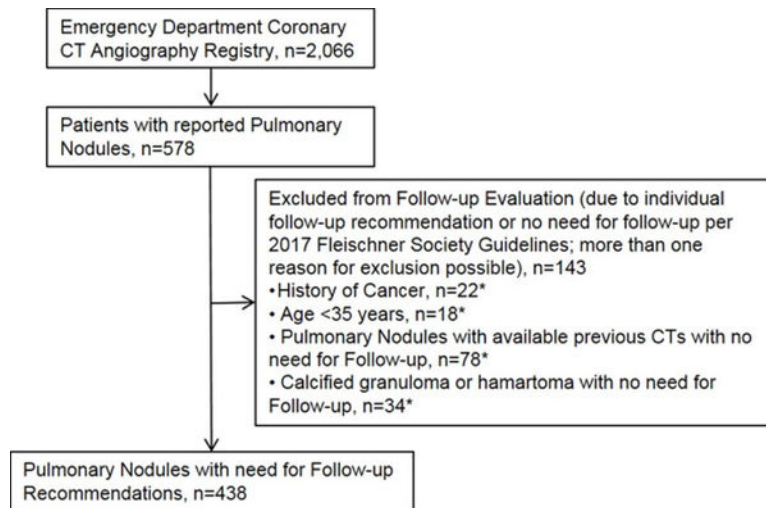


Fig 2. Flow chart of patients with incidentally detected pulmonary nodules within the registry of acute chest pain patients who underwent coronary CT angiography.

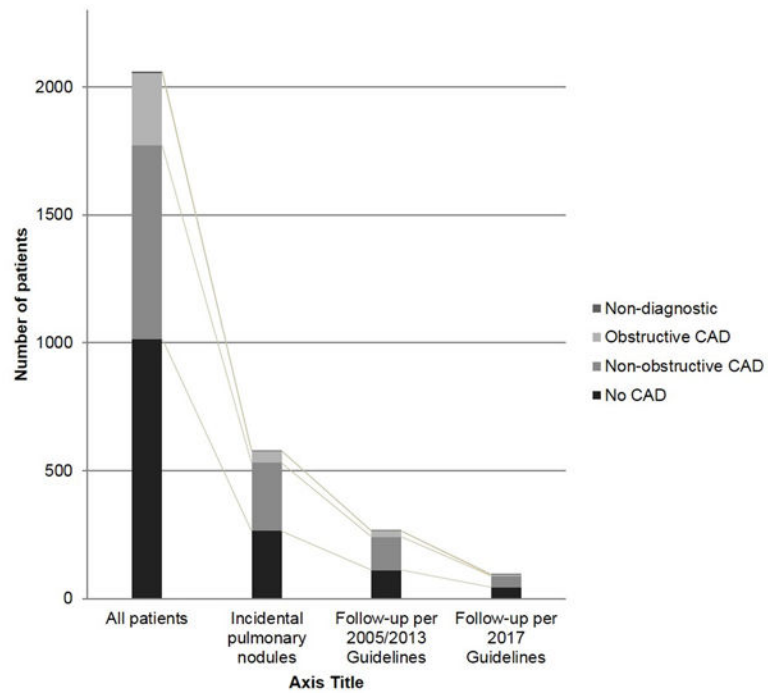


Fig 3. Patients with recommended follow-ups of incidental pulmonary nodules based on prior (2005 and 2013) and currently revised (2017) Fleischner Society Guidelines compared to all patients, subdivided into coronary artery disease severity.

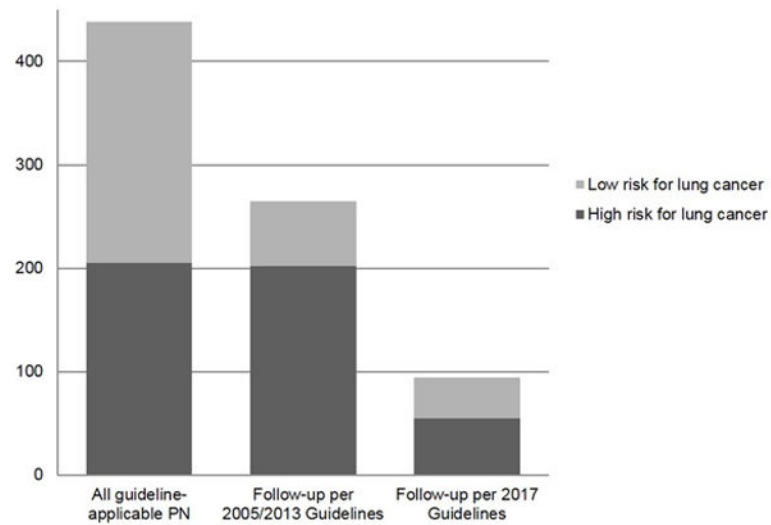


Fig 4. Patients with incidental pulmonary nodules and need for follow-up testing per prior (2005 and 2013) and revised (2017) Fleischner Society Guidelines subdivided into low and high risk for lung cancer. High risk for lung cancer included history of smoking, age >60 years, upper lobe location of PN, irregular morphology PN, and PN size >20 mm.

Table 1

Baseline characteristics

Characteristics	Patients with need for pulmonary nodule follow-up evaluation n=438
Age (years)	54.5 ± 11.0
Female	190 (43.4)
Male	248 (56.6)
Race	
Caucasian	298 (68.0)
African-American	46 (10.5)
Asian	9 (2.1)
Other/Unknown	85 (19.4)
Hispanic Ethnicity	44 (10.0)
BMI (kg/m ²)	29.7 ± 6.3
Cardiovascular risk factors	
Past or current smoker	123 (28.1)
Current smoker	37 (8.4)
Diabetes Mellitus	41 (9.4)
Dyslipidemia	126 (28.8)
Hypertension	168 (38.4)
Family history of CAD	81 (18.5)
History of cancer	–

Values are mean ± standard deviation or n (%)

BMI, body mass index; CAD, coronary artery disease

Table 2

Fleischner Society Guidelines-applicable pulmonary nodule management classified per pulmonary nodule characteristics (type, number, and size) and lung cancer risk.

Characteristics	No. of patients with PN n (%)	Recommendation for PN follow-up testing per guidelines (minimal no. of chest CTs)			2017	No. of patients with recommended follow-up CT		Difference %
		2005/2013	2017	2005/2013		2017		
All	438 (100)				264	94	-64.5*	
Low risk	233(53.2)				63	39	-38.1*	
High risk	205 (46.8)				201	55	-72.8*	
Solid PN (Single and multiple)	398 (90.9)				231	64	-72.3*	
Low risk	219 (50.0)				52	28	-46.2*	
High risk	179 (40.9)				179	36	-80.0*	
4 mm	288(65.8)				121	-		
Low risk	167 (38.1)	No	No		-	-		
High risk	121 (27.6)	Yes (1)	No		121	-		
5 mm	46 (10.5)				46	-		
Low risk	24 (5.5)	Yes (1)	No		24	-		
High risk	22 (5.0)	Yes (1)	No		22	-		
6-8 mm	54 (12.3)				54	54		
Low risk	24 (5.5)	Yes (1-2)	Yes (1)		24	24		
High risk	30 (6.8)	Yes (2-3)	Yes (2)		30	30		
>8 mm	10 (2.3)				10	10		
Low risk	4 (0.7)	Yes (3***)	Yes (1-2**)		4	4		
High risk	6 (1.4)	Yes (3***)	Yes (1-2**)		6	6		
Subsolid PN	40 (9.1)				34	30	-11.8*	
Low risk	14 (3.2)				11	11	0.0	
High risk	26 (5.9)				23	19	-17.4*	
<i>Single subsolid PN</i>	24 (5.5)				18	14		
Pure ground glass PN	21 (4.8)				15	12		

Characteristics	No. of patients with PN n (%)	Recommendation for PN follow-up testing per guidelines (minimal no. of chest CTs)		No. of patients with recommended follow-up CT		Difference %
		2005/2013	2017	2005/2013 n	2017 n	
<5 mm	6 (1.4)	No	No	–	–	
5 mm	3 (0.7)	Yes (4)	No	3	–	
6 mm	12 (2.7)	Yes (4)	Yes (6)	12	12	
Partly solid PN	3 (0.7)			3	2	
<5 mm	0	Yes (4)	No	0	–	
5 mm	1 (0.2)	Yes (4 ^{**})	No	1	–	
6 mm	2 (0.5)	Yes (4 ^{**})	Yes (6)	2	2	
<i>Multiple subsolid PN</i>	16 (3.7)			16	16	
<6 mm	10 (2.3)	Yes (2 ^{**})	Yes (3)	10	10	
6 mm	6 (1.4)	Yes (1–4 ^{**})	Yes (1 ^{**})	6	6	

Values are n (%).

CT, computed tomography; PN, pulmonary nodule

* p<0.05

**

Further examinations (PET, biopsy) might be necessary in addition to chest CT based on the 2005, 2013, and 2017 Fleischner Society Guidelines

Table 3

Detection of pulmonary nodules which are applicable to the Fleischner Society Guidelines, subdivided into coronary artery disease severity by coronary CTA and lung cancer risk.

Findings	Registry	No. of patients with need for PN follow-up (% ^{***})	No. of patients with need for PN follow-up		Minimal total no. of follow-up chest CT ^{***}	
			2005/2013 n (% ^{***})	2017 n (% ^{***})	2005/2013 n	2017 n
All	2,066	438 (21.2)	94 (4.5)	430	190	-55.8*
Low risk		233	39	108	64	-40.1*
High risk		205	55	322	126	-60.9*
No CAD	1014	202 (19.9)	44 (4.3)	177	74	-58.2*
Low risk		130	24	57	32	-43.9*
High risk		72	20	120	42	-65.0*
Non-obstructive CAD	757	203 (26.8)	44 (5.8)	215	99	-54.0*
Low risk		92	13	44	25	-43.2*
High risk		111	31	171	74	-56.7*
Obstructive CAD	281	32 (11.4)	5 (1.8)	36	16	-55.6*
Low risk		10	1	5	6	20.0
High risk		22	4	31	10	-67.7*
Non-diagnostic	9	1 (11.1)	1 (11.1)	2	1	-50.0
Low risk		1	1	2	1	-50.0
High risk		0	0	0	0	-

Values are n (%), differences are in %

CAD, coronary artery disease; PN, pulmonary nodule

No CAD, no coronary artery stenosis nor plaque; Non-obstructive CAD, 1-69% stenosis or left main coronary artery 1-49% stenosis; Obstructive CAD, 70% stenosis or left main coronary artery 50% stenosis;

Low risk for lung cancer: age < 60 years, no current smoker, PN not within upper lobe, no irregular or spiculated morphology of PN

High risk for lung cancer: age > 60 years, current smoker, PN in upper lobe location; irregular or spiculated morphology of PN

* p<0.05

** In percentage to total number of patients per CAD category

Further examinations (PET, biopsy) might be necessary in addition to chest CT based on the 2005, 2013, and 2017 Fleischner Society Guidelines

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Table 4

Extra-cardiac findings in coronary CT angiography.

Characteristics	Emergency Department Coronary CT Angiography Registry n=2,066
Pulmonary findings	
Pulmonary nodules	578 (28.0)
Pulmonary embolism	6 (2.9)
Pneumonia	13 (6.3)
Pneumonitis	2 (0.1)
Pleural effusion	30 (1.5)
Aortic dissection	4 (0.2)
GERD	29 (1.4)
Tumor	3 (0.1)
Newly detected malignancies	2 (0.1)
Esophageal cancer	1 (0.0)
Cholangiocarcinoma	1 (0.0)
Non-specific paraoesophageal mass	1 (0.0)

Values are n (%)

GERD, gastroesophageal reflux disease

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