Research Article

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Incidence, Risk Factors, and Patient Management of Incidental Coronary Artery Calcification on Non-ECG Gated Computed Chest Tomography: A Systematic Review

Rohanlal Vishwanath[1], Sarah Gorgis[2], Varinder Singh[3], James Iordanou[4], Hayk Papukhyan[5], Aeman Hana[6], Cori Russell[2], Karthikeyan Ananthasubramaniam[7]

[1]*Department of Internal Medicine, Cleveland Clinic Foundation, Cleveland, Ohio, USA.*

[2]*Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan, USA.*

[3]*Michigan State University, College of Osteopathic Medicine, East Lansing, Michigan, USA.*

[4]*Department of Internal Medicine, Hurley Medical Center, Flint, Michigan, USA.*

[5]*Department of Internal Medicine, Henry Ford Macomb, Clinton, Michigan, USA.*

[6]*Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.*

[7]*Division of Cardiovascular Medicine, Henry Ford West Bloomfield Hospital, West Bloomfield, Michigan, USA.*

***Correspondence:**
Karthikeyan Ananthasubramaniam, MD FACC FASE FASNC FSCCT FSCMR FRCP Professor of Medicine, Wayne State University, Cardiovascular Department, Henry Ford Hospital 2799 W Grand Blvd, Detroit, MI 48202, Tel: 313-916-2721.

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ABSTRACT

Coronary artery calcification (CAC) is an independent predictor of cardiovascular events and can be reliably detected on non-Electrocardiogram (ECG) gated computed tomography (CT) scans. The increased use of CT has made CAC a common incidental finding, although the frequency remains variable in published literature. We aimed to identify the incidence of CAC found on routine non-ECG gated CT scans, risk factors associated with these findings, and management outcomes that resulted from discovery of CAC. A systematic review was conducted through literature search using predetermined search criteria. Applicable studies were screened by 3 investigators for eligibility. Data regarding indication for CT imaging, presence of CAC, cardiovascular risk factors, and management outcomes was collected. A total of 3585 study subjects were included for review. CAC was found in 31.2% (n = 1118) patients. Indications for CT imaging were 33.0% lung cancer screening, 16.0% for intrapulmonary pathology, and 50.0% for other reasons. In patients with CAC, the average age was 61.5 $\pm$ 8.8 years old, 77.2% were male, 41.4% were smokers, 32.2% had hypertension, 31.5% had hyperlipidemia, and 11.2% had diabetes. Patients with CAC were older ($p < 0.001$), more likely to be smokers ($p = 0.002$), and more likely to have hyperlipidemia ($p < 0.001$). The presence of CAC in reports did not significantly alter management plans. In conclusion, traditional cardiovascular risk factors are associated with incidental CAC. Not reporting incidental CAC is a missed opportunity for identification of patient at increased risk of cardiovascular events in the community.

Keywords
Incidental, Coronary artery calcification, Non-ECG gated, CT scan.

List of Abbreviations
CAC: Coronary Artery Calcification; CAD: Coronary Artery Disease; CT; Computed tomography; ECG: Electrocardiogram.

Introduction
Cardiovascular disease has been the leading cause of death worldwide for the last 15 years [1]. In the United States, the incidence of myocardial infarctions in 2019 was 1,055,000, with 720,000 new attacks and 335,000 recurrent attacks [1]. Cardiovascular disease accounted for 840,786 deaths in 2016 in the United States alone [1]. Despite significant advancements in risk stratification, medical optimization, and treatment of coronary disease, the rates continue to rise. Every effort should be made to identify coronary artery disease (CAD) early using the available tools we have. Coronary artery calcification (CAC) is an independent risk factor for CAD and has been found to positively correlate with future cardiovascular disease [2-5]. Electrocardiogram (ECG)-gated computed tomography (CT) scans were initially used for calculation of CAC scores using the Agatston method to identify and risk stratify patients with visualized coronary calcium [6]. The recent American College of Cardiology/American Heart Association prevention guidelines have given coronary calcium estimation a class IIb indication when risk assessment by traditional risk scores fall in the "gray zone" [7]. However, calcium scoring is currently not covered by most insurances. This significantly impedes its routine use as it becomes an out-of-pocket patient expenditure.

Thus, identification of CAC on non-ECG gated CT scans performed for other purposes serves as an attractive option for visual atherosclerotic burden assessment [8,9] and can potentially impact patient diagnosis and management downstream [10]. We performed a systematic review of current literature to identify studies evaluating the incidence of CAC on non-ECG gated chest CTs. We also sought to assess whether there is correlation between incidental CAC and risk factors for CAD, determine what clinical decisions were made regarding these incidental findings, and provide a summary recommendation in reporting and acting on incidental CAC.

Materials and Methods
This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta- Analysis (PRISMA) guidelines. The study was initially planned and designed by two researchers. Main outcome markers of this study were outlined, and literature searches were executed.

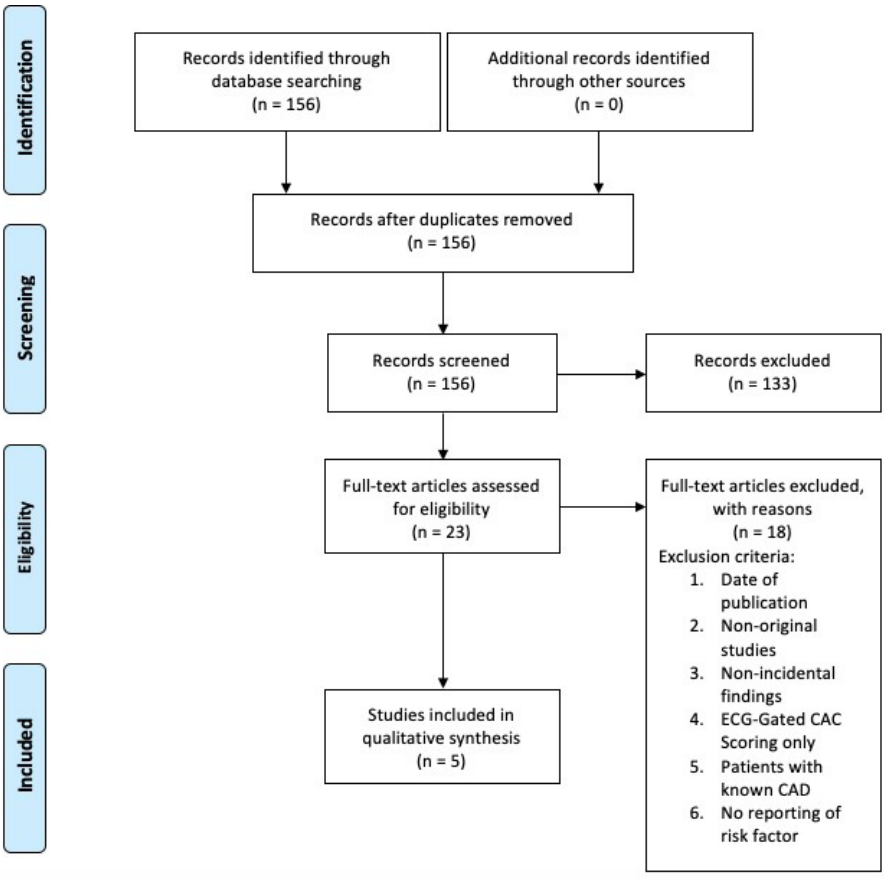

Figure 1: Outline of literature search for original studies from 2008-2019, assessing incidence of CAC and risk factors associated with incidental CAC detected on routine non-ECG gated CT scans.

We performed 2 sets of literature searches in the following sources: Medline, Google Scholar and review of publications cited in current literature. The first was conducted using the following keywords search string: coronary artery calcification AND incidental AND CT scans (Figure 1). In total, 156 studies were found. The second part of the search was conducted using the following keywords: incidental coronary artery calcification AND physician decisions AND medications AND compliance (Figure 2). In total, 214 studies were found. For both sets of searches, studies between January 1, 2008- December 31, 2019 were included for further review. These searches were performed in August 2019. Only original studies, in the English language, were selected, while review articles, meta-analysis, editorials, and letters were excluded. With the remaining studies, duplicates were checked and removed. In the end, 246 studies were further reviewed and assessed for inclusion of incidental CAC, risk factors in patients with no known CAD, and impact of incidental CAC on medical management and physician decision making. Studies were excluded if CAC was formally evaluated and quantitated, ECG-gated CT scans were used, non-ECG gated CT scans were used for assessment of cardiac findings, or if studies were published before 2008 or after 2019.

Data regarding study population, incidental CAC, and risk factors were recorded. Data regarding cardiovascular outcomes recorded in the respective studies in patients with and without CAC were also included in this review. For the second set of studies, we focused on identifying how CAC affected physician decision making regarding follow-up care and medication changes.

Demographics, baseline characteristics, and clinical outcomes were evaluated. Numerical variables were described as mean and standard deviation, while discrete variables were described as proportions. Continuous variables were compared using Student's t-test while categorical variables were compared using the chi-squared test. The one-way analysis of variance was used to determine any statistical significance between the means of 3 or more independent groups. Statistical analyses were considered significant if $p < 0.05$.

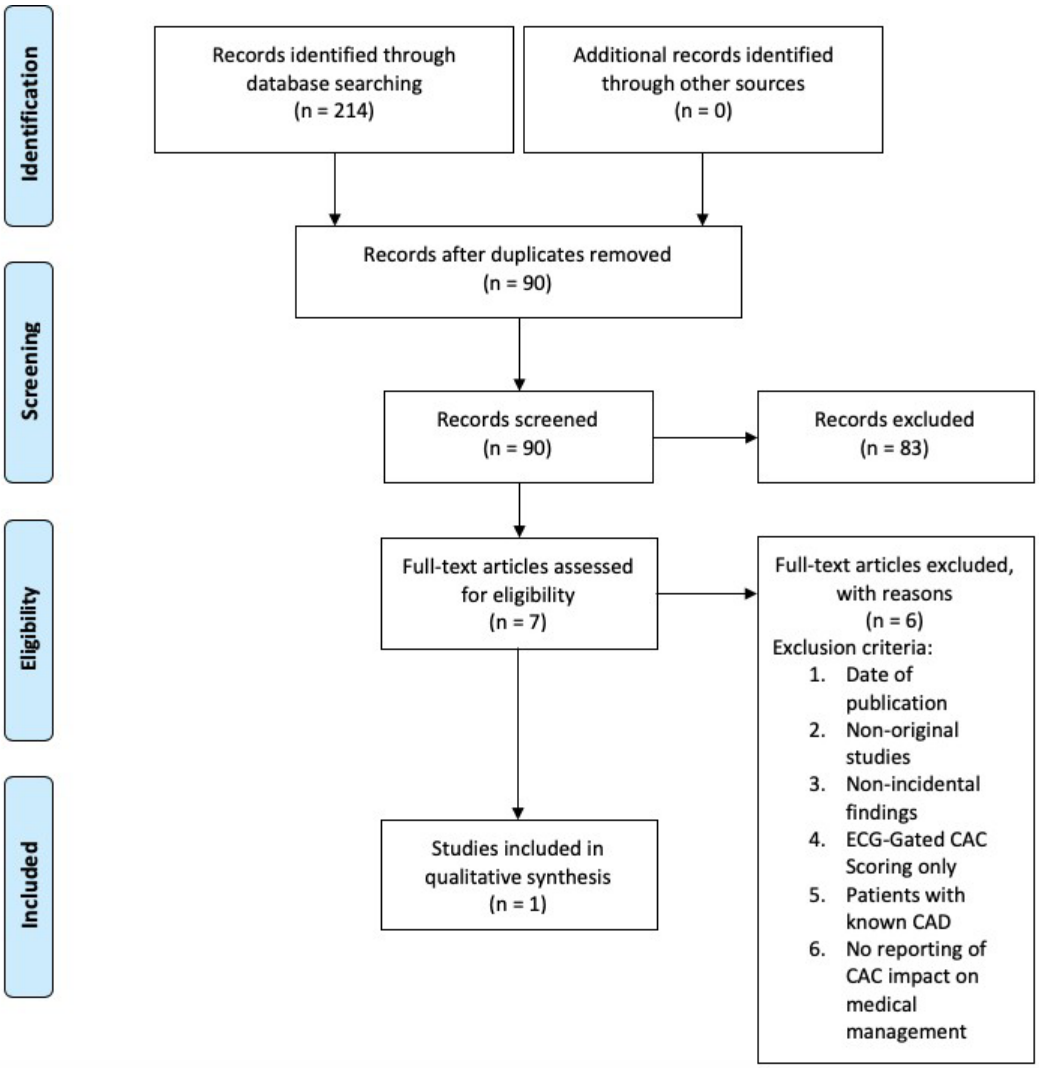

Figure 2: Outline of literature search for original studies from 2008-2019, assessing changes in medical management for patients in whom incidental CAC was detected on routine non-ECG gated CT scans.

Results

Six studies were included in the final review; 5 which assessed the rate of incidental CAC and 1 which reported data on outcomes and decisions made on the incidental findings. Four studies were retrospective in design, 1 was a case-cohort study, and 1 was a prospective study (Table 1). All studies excluded patients who had known history of CAD and those who had CT scans ordered to evaluate coronary calcium. Indications for CT imaging were routine lung cancer screening (2 studies), ruling out intrapulmonary process in patients with chest pain (1 study), and various other non-cardiac indications (3 studies) (Table 1).

A total of 3585 patients were included in the final analysis. Incidental CAC was reported in 31.2% of patients (n = 1118) with no documented history of CAD (Table 1). Patients with detectable CAC had an average age of 61.5 ± 8.8 years; 77.2% were male, 41.4% were smokers, 32.2% had hypertension, 31.5% had hyperlipidemia, and 11.2% had recorded diabetes (Table 1). When compared to patients without detectable CAC, those with CAC were older (61.5 ± 8.8 vs 54.5 ± 7.7 years, $p < 0.001$), more likely to use tobacco (51.5% vs 41.4%, $p = 0.002$), and more likely to have hyperlipidemia (31.5% vs 15.2%, $p < 0.001$). There was no statistically significant difference in gender, presence of hypertension, or presence of diabetes (Table 2).

One study in the analysis evaluated physician awareness and medical management of patients in which CAC was found incidentally [13]. Uretsky et. al reported CAC was reported in 35.9% of patients (74/206) in this study. Out of 132 referring providers, 22.7% (30/132) were aware of the reported CAC, 53.8% (71/132) believed it should be treated as CAD, and only 4.5% (6/132) made medication changes based on this information [13]. There were no statistically significant changes made to medications after learning about the CAC [13]. In addition, cardiology consultation consideration was evaluated for both inpatient and outpatient settings. After discovery of CAC, 12.0% of providers referred patients for outpatient cardiology evaluation, 7.0% of providers initiated an inpatient consult, and 79.0% of providers did not refer patients to cardiology [13].

Discussion

In this systematic review, incidental CAC was reported in 31.2% of the 3585 patients without known CAD who underwent non-ECG gated CT scans done for non-coronary purposes. Patients with incidental CAC were more likely to be older, tobacco users, and have hyperlipidemia.

Traditionally, ECG-gated CT scans have been used for calculation of a CAC score to risk stratify patients for underlying CAD,[6]. Advancements and availability of modern non-ECG gated CT scans performed for non- cardiac indications have resulted in increased identification of incidental CAC findings [8-10]. Identification of incidental CAC on non-ECG gated CT scans is done through the "ordinal method", which is a visual quantification and scoring of calcifications. The ordinal method has been shown to correlate with the Agatston method used in ECG-gated CT scans. In a study by Azour et al., there was a positive correlation of increasing ordinal scale score with increasing mean Agatson score with a Pearson correlation of $R = 0.811$, $p < 0.01$ [8]. The sensitivity and specificity of non-ECG gated CT scans in detecting CAC when compared to ECG-gated CT scans has been shown to be 96.5% and 100%, respectively [16]. There are two available

Table 1: Incidence of Coronary Artery Calcification and Rate of Comorbidities by Study

Author	Year	Study Type	CT Indication	Study population (N)	Incidence of CAC N (%)	Average Age (mean ± STD)	Male (%)	Smoking (%)	HTN (%)	HLD (%)	Diabetes (%)
Hiltunen	2008	Retrospective	Lung cancer screening	505	488 (96.7%)	61.0 ± 7.2	96.6	-	23.0	-	7.0
Gondrie	2010	Case-Cohort	Various reasons	1723	155 (8.9%)	61.5 ± 16.1	58.0	-	-	-	-
Uretsky	2015	Prospective	Various reasons	204	74 (36.3%)	-	-	-	-	-	-
Shao	2017	Retrospective	Intrapulmonary pathology	410	200 (48.7%)	64.3 ±9.4	46.0	43.8	43.0	31.5	19.0
Lichtenstein	2018	Retrospective	Various reasons	162	19 (11.7%)	41.5 ± 6.7	84.0	33.6	-	-	-
Reiter	2018	Retrospective	Lung cancer screening	581	182 (31.3%)	61.6 ± 6.4	75	43.0	45.0	-	14.0
				Total 3585	**Total** 1118 (31.2%)	**Avg** 61.5 ± 8.8	**Avg** 77.2%	**Avg** 41.4%	**Avg** 32.2%	**Avg** 31.5%	**Avg** 11.2%

Abbreviations: *CAC- Coronary Artery Calcification, HTN- Hypertension, HLD- Hyperlipidemia.*

Table 2: Comparison of Age, Gender, and Comorbidities in Patients with and without Coronary Artery Calcification

	Coronary Artery Calcification		
	Present	**Absent**	**P value**
Age (mean ± STD)	61.5 ± 8.8	54.5 ± 7.7	<0.001
Male	77.2%	75.8%	0.6
Tobacco use	51.5%	41.4%	0.002
Hypertension	32.2%	28.7%	0.2
Hyperlipidemia	31.5%	15.2%	<0.001
Diabetes Mellitus	11.2%	8.7%	0.1

studies that compare CAC severity in patients who received both types of scans; Wu et al. showed that 63% of visually estimated scores were within the same category as ECG-gated scans [17], and Kim et al. showed that 71.6% of visual rankings were in the same category as ECG- gated scans [18]. This data suggests that non-ECG gated CT scans can reliably serve as an additional tool for early identification of atherosclerotic burden, especially given the strong correlation with ECG-gated scans, lower radiation dose, and volume performed annually.

CAC is an independent predictor of adverse cardiovascular events [2-4]. In our systematic review, 5 of the 6 studies analyzed clinical outcomes of patients with detected CAC and found that CAC positively correlated with future cardiovascular events. The number of vessels involved [11], density of calcium [4,19], and presence of calcified valves [12] were all significantly associated with likelihood of future cardiovascular disease. When compared to traditionally utilized risk assessment calculators, such as the Framingham Risk Score, CAC severity positively correlated with low, medium, and high Framingham Risk Score [14]. More recently, a retrospective study showed that incidental CAC is independently predictive of survival in cancer patients undergoing positron emission tomography-CT for oncologic purposes [20] (Supplemental table).

Despite the association of incidental CAC identification with cardiovascular outcomes, a significant number of providers are unaware of the findings, and those who are aware do not make significant management changes [13]. In a different study assessing provider awareness, CAC was reported in 36.0% of the study population, comparable to our study prevalence. Out of 132 referring providers, 30 were aware of the reported CAC; of those 30, 16 thought this should be treated as CAD but only 1 made medication changes. In addition, the majority of providers did not refer patients for cardiology evaluation. This represents a disconnect between easily available information alerting clinicians of atherosclerosis and therapeutic inertia for proactive action (i.e., initiation of statin therapy or getting an opinion from cardiology). Although there is no randomized trial to date comparing outcomes of statin initiation versus no statin initiation in asymptomatic patients with CAC, there is abundant non-randomized data of CAC as a future predictor of cardiovascular risk. Hence, aggressive primary prevention strategies and shared decision making on statin initiation is logical and recommended. Although calcium score cut-offs have been used in guidelines for statin initiation, the presence of visual calcium on non-ECG gated scans can serve as a simple alternative for decisions on risk reduction strategies of long-term adverse cardiac events.

The reporting of incidental CAC on non-gated CT scans continues to be highly variable and is left to reader discretion. In one study, incidental CAC was found in 68.9% (254/369) of patients but was only reported in 49.3% of patients. In those with reported CAC, 31.0% did not report CAC severity, despite visual assessment of calcification severity being a reliable predictor of future cardiovascular events [15]. In another study, incidental CAC was identified in 58.3% (207/355) of patients, but only reported in the final radiology report of 44.0% of the cases [21]. In a study evaluating patients with chest pain and incidentally discovered CAC, 55% of patients had CAC reported under "findings", but only 8.0% of patient reports had CAC noted in the final "impressions" section of the report [22]. Although it is underreported, there is evidence of strong reproducibility between experienced radiologists in identifying CAC on these scans [18].

The 2016 Society of Cardiovascular Computed Tomography/ Society of Thoracic Radiology guidelines have recommended that professional societies of radiology and cardiovascular medicine should provide standardized guidelines in reporting and managing incidental CAC [6]. The 2016 Society of Cardiovascular Computed Tomography/Society of Thoracic Radiology guidelines provide recommendations in reporting CAC and severity based on both the Agatston method and ordinal method. For ordinal scoring, they recommend the following risk stratification in reporting CAC; 0 = very low risk, 1-3 = mild to moderate increased risk, and 4-12 = moderate to severely increased risk [6]. Standardizing the reporting of incidental CAC can provide radiologists with foundations on which to report CAC. Additionally, there needs to be improved clinician awareness of the presence of CAC, in order to improve identification and modification of cardiovascular risk factors. Cardiovascular disease continues to be the leading cause of death in the United States. Given the millions of routine CT scans performed each year, incidental CAC is a missed opportunity for primary prevention.

Limitations

Although our study provides evidence for the importance of incidental CAC, this present study has some limitations. Most of the studies included in this review are retrospective in nature. Due to the inherent limitations of retrospective analysis, our conclusions cannot be made causational, rather, they should be considered correlational. Many of the studies included in this review lacked complete data sets regarding cardiovascular risk factors, and a few studies only reported the presence of risk factors in patients with CAC. Finally, studies included in this review have varying cohorts and sample sizes, which, can introduce selection bias.

Conclusion

CAC is an independent risk factor of CAD, which can be reliably detected on non-ECG gated CT scans.

Incidental CACs on non-ECG gated CT scans are common and should be systematically reported. Lack of incidental CAC reporting and awareness is a missed opportunity to identify patients who have increased of future cardiovascular events.

References

1. Benjamin EJ, Muntner P, Alonso A, et al. American Heart Association Council on Epidemiology and Prevention Statistics Committee, Stroke Statistics Subcommittee. Heart

disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation. 2019; 139: e56-e528.

2. Shao L, Yan AT, Lebovic G, et al. Prognostic value of visually detected coronary artery calcification on unenhanced non-gated thoracic computed tomography for prediction of non-fatal myocardial infarction and all-cause mortality. J Cardiovasc Comput Tomogr. 2017; 11: 196-202.
3. Jacobs PC, Prokop M, van der Graaf Y, et al. Comparing coronary artery calcium and thoracic aorta calcium for prediction of all-cause mortality and cardiovascular events on low-dose non-gated computed tomography in a highrisk population of heavy smokers. Atherosclerosis. 2010; 209: 455-462.
4. Jacobs PC, Gondrie MJ, van der Graaf Y, et al. Coronary artery calcium can predict all-cause mortality and cardiovascular events on low-dose CT screening for lung cancer. AJR Am J Roentgenol. 2012; 198: 505-511.
5. Rasmussen T, Kober L, Abdulla J, et al. Coronary artery calcification detected in lung cancer screening predicts cardiovascular death. Scand Cardiovasc. 2015; 49: 159-167.
6. Hecht HS, Cronin P, Blaha MJ, et al. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: a report of the 12 Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. J Cardiovasc Comput Tomogr. 2017; 11: 74-84.
7. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019; 74: 1376-1414.
8. Azour L, Kadoch MA, Ward TJ, et al. Estimation of cardiovascular risk on routine chest CT: ordinal coronary artery calcium scoring as an accurate predictor of Agatston score ranges. J Cardiovasc Comput Tomogr. 2017; 11: 8-15.
9. Jacobs PC, Mali WP, Grobbee DE, et al. Prevalence of incidental findings in computed tomographic screening of the chest: a systematic review. J Comput Assist Tomogr. 2008; 32: 214-221.
10. Pakdaman MN, Rozanski A, Berman DS. Incidental coronary calcifications on routine chest CT: clinical implications. Trends Cardiovasc Med. 2017; 27: 475-480.
11. Hiltunen A, Kivisaari L, Leino-Arjas P, et al. Visual scoring of atherosclerosis in chest computed tomography: findings among male construction workers. Acta Radiol. 2008; 49: 328-336.
12. Gondrie MJ, van der Graaf Y, Jacobs PC, et al. The association of incidentally detected heart valve calcification with future cardiovascular events. Eur Radiol. 2011; 21: 963-973.
13. Uretsky S, Chokshi N, Kobrinski T, et al. The interplay of physician awareness and reporting of incidentally found coronary artery calcium on the clinical management of patients who underwent noncontrast chest computed tomography. Am J Cardiol. 2015; 115: 1513-1517.
14. Lichtenstein G, Perlman A, Shpitzen S, et al. Correlation between coronary artery calcification by non-cardiac CT and Framingham score in young patients. PLoS One. 2018; 13: e0195061.
15. Reiter MJ, Nemesure A, Madu E, et al. Frequency and distribution of incidental findings deemed appropriate for S modifier designation on low-dose CT in a lung cancer screening program. Lung Cancer. 2018; 120: 1-6.
16. Hutt A, Duhamel A, Deken V, et al. Coronary calcium screening with dual-source CT: reliability of ungated, high-pitch chest CT in comparison with dedicated calciumscoring CT. Eur Radiol. 2016; 26: 1521-1528.
17. Wu MT, Yang P, Huang YL, et al. Coronary arterial calcification on low-dose ungated MDCT for lung cancer screening: concordance study with dedicated cardiac CT. AJR Am J Roentgenol. 2008; 190: 923-928.
18. Kim YK, Sung YM, Cho SH, et al. Reliability analysis of visual ranking of coronary artery calcification on low-dose CT of the thorax for lung cancer screening: comparison with ECG-gated calcium scoring CT. Int J Cardiovasc Imaging. 2014; 2: 81-87.
19. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol. 2007; 49: 1860-1870.
20. Mais HE, Kay R, Almubarak H, et al. Prognostic importance of coincidental coronary artery calcification on FDG-PET/CT oncology studies. Int J Cardiovasc Imaging. 2021; 37: 1479-1488.
21. Williams KA Sr, Kim JT, Holohan KM. Frequency of unrecognized, unreported, or underreported coronary artery and cardiovascular calcification on noncardiac chest CT. J Cardiovasc Comput Tomogr. 2013; 7: 167-172.
22. Johnson C, Khalilzadeh O, Novelline RA, et al. Coronary artery calcification is often not reported in pulmonary CT angiography in patients with suspected pulmonary embolism: an opportunity to improve diagnosis of acute coronary syndrome. AJR Am J Roentgenol. 2014; 202: 725-729.