Thèse d'exercice

Université de Limoges

Faculté de Médecine

Année 2024 Thèse N°

Thèse pour le diplôme d'État de docteur en Médecine

Présentée et soutenue publiquement

le 27 mars 2024

Par Guillaume SIGNORET

Prognostic value of incidental coronary artery calcium in CT pulmonary angiography for suspected pulmonary embolism

Thèse dirigée par le Docteur Marouane Boukhris

Examinateurs :

M. le Professeur Victor Aboyans, PU-PH, CHU Limoges	Président
M. le Docteur Marouane Boukhris, PH, CHU Limoges	Directeur
M. le Professeur Aymeric Rouchaud, PU-PH, CHU Limoges	Juge
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Aux membre du jury :

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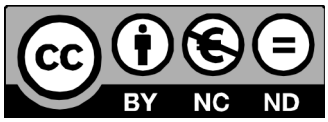

Liste des abréviations

AI : *Artificial intelligence*

ACS: *Acute coronary syndrome*

ASCVD: *Atherosclerotic cardiovascular disease*

CAC: *Coronary artery calcifications*

CAD: *Coronary artery disease*

CKD: *Chronic kidney disease*

CT: *Computed tomography*

CTPA: *CT pulmonary angiography*

CV: *Cardiovascular*

DL: *Deep learning*

ECG: *Electrocardiogram*

eGFR: *Estimated glomerular filtration rate*

HF: *Heart failure*

HR: *Hazard ratio*

LDLc: *Low density lipoprotein-cholesterol*

MI: *Myocardial infarction*

NLST: *National lung screening trial*

PAD: *Peripheral artery disease*

PE: *Pulmonary embolism*

SD: *Standard deviations*

TIA: *Transient ischemic attack*

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I. INTRODUCTION

Coronary artery calcifications (CAC) are an indicator of atherosclerosis reflecting the presence of coronary artery disease (CAD). The CAC score determined by computed tomography (CT) has emerged as a non-invasive method to stratify the risk for major cardiac events in asymptomatic individuals[1]. It provides a direct measure of an individual's burden of subclinical atherosclerosis and is strongly associated with the risk for cardiovascular events and all-cause mortality[2]. Furthermore, the American College of Cardiology/American Heart Association prevention guidelines recommend consideration of CAC scoring among patients with a borderline to intermediate 10-year atherosclerotic cardiovascular disease (ASCVD) risk score in the decision-making process to prescribe preventive therapies and follow beneficial lifestyle changes[3].

Each year, millions of chest CT scans are widely performed for the diagnosis of several thoracic and pulmonary diseases. For instance in 2016, 12.7 million CT chest scans were performed in the United States versus only ~ 57,000 ECG-gated CAC scores[4]. Subsequently, a great interest has been recently raised towards CAC severity estimation in non-gated chest-CT examinations. This is an opportunistic approach to detect incidentally CAC by simple visual ordinal classification of CAC (not requiring dedicated software), which has been shown to be well correlated with the Agatston scoring method[5] and able to predict cardiovascular prognosis in different clinical settings such as lung cancer screening programs[6] or during the COVID-19 outbreak period[7].

CT pulmonary angiography (CTPA) is indicated to confirm the diagnosis in patients with suspected pulmonary embolism (PE) and could represent a new opportunity to assess CAC visually.

The purpose of our study was to investigate the association between incidental visual CAC evaluation during CTPA and mid-term cardiovascular events in patients suspect for PE.

II. METHODS

II.1. Study population

This is a retrospective single center study. All consecutive patients who underwent CTPA for suspected PE at emergency department of CHU Dupuytren Limoges, France between January 1st and December 31st, 2017, were considered for this study. Patients aged <40 years, those with known CAD, those with acute coronary syndrome (ACS) and those who died during hospital stay were excluded.

Patients with PE were treated according to standards of care[8].

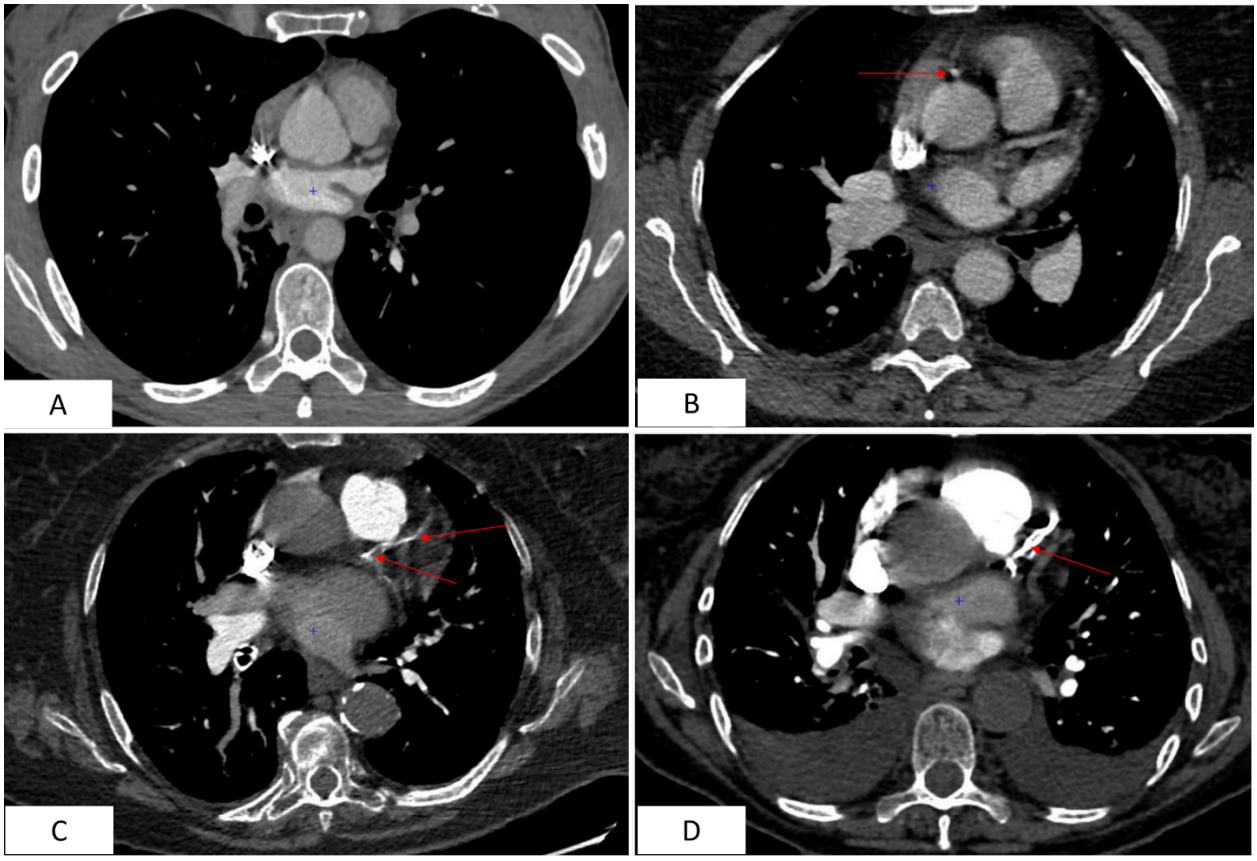
II.2. Visual scale for CAC scoring in CTPA

All examinations were carried out on the same CT scan (General Electric Optima model CT660) installed in 2016. The voltage (80-120 kV) and intensity (120-400 mA) of the X-rays were automatically selected according to the patient's morphotype. Helical acquisitions were carried out from the shoulders to the adrenals in apnea at maximum inspiration without cardiac gating, with a cutting thickness of 1.375 mm and an interval between cuts of 0.625 mm. The iodinated contrast product was injected at a flow rate of 3.5 ml/s for a volume of 55 ml.

CAC scoring was performed independently of care by an expert radiologist in cardiothoracic imaging (8 years of experience) and blinded from all clinical data. Incidental CAC evaluation was performed according to the British guidelines[9]: the extent and severity of CAC was measured on a per patient basis and labelled as none (grade 0), mild (grade 1), moderate (grade 2) and severe (grade 3). Examples of visual CAC scoring are shown in Figure 1. The cohort was then subdivided accordingly into 4 subgroups.

In patients with confirmed PE further assessment by two senior residents blinded from all clinical data (one in cardiology and one in radiology, both in their fourth year of residency), was performed to assess inter-observer agreement.

Figure 1. Visual CAC scoring in CTPA: A) none (grade 0); B) mild (grade 1); C) moderate (grade 2); D) severe (grade 3)



Red arrows indicate CAC.

Abbreviations. CAC=coronary artery calcifications; CTPA=Computed tomography pulmonary angiography

II.3. Outcomes and definitions

Follow-up data were collected through electronic medical records and referring cardiologists/general practitioners.

The primary outcome was a composite of cardiovascular mortality, myocardial infarction (MI) or coronary revascularization. The secondary outcomes were all-cause mortality, and an extended composite outcome including cardiovascular mortality, MI, coronary revascularization, ischemic stroke, ischemic peripheral events and hospitalization for heart failure.

MI was defined according to the current fourth universal definition of MI[(10)].

Ischemic peripheral event included amputation, development of critical ischemia, acute aortic dissection and rupture of abdominal aneurysm.

II.4. Statistical analysis

Kappa(κ)-statistic test was used to evaluate inter-observer agreement for 4-stage CAC classification, as well the detection of moderate to severe coronary calcifications (grade 2/3, vs. grade 0/1) in patients with confirmed PE between senior radiologist, radiology and cardiology residents.

Categorical variables were presented as numbers of percentages and were compared using the Chi2 test (expected the frequency > 5) or Fisher's exact test, as appropriate. Continuous variables were presented as means ± standard deviations (SD) or medians and interquartile intervals.

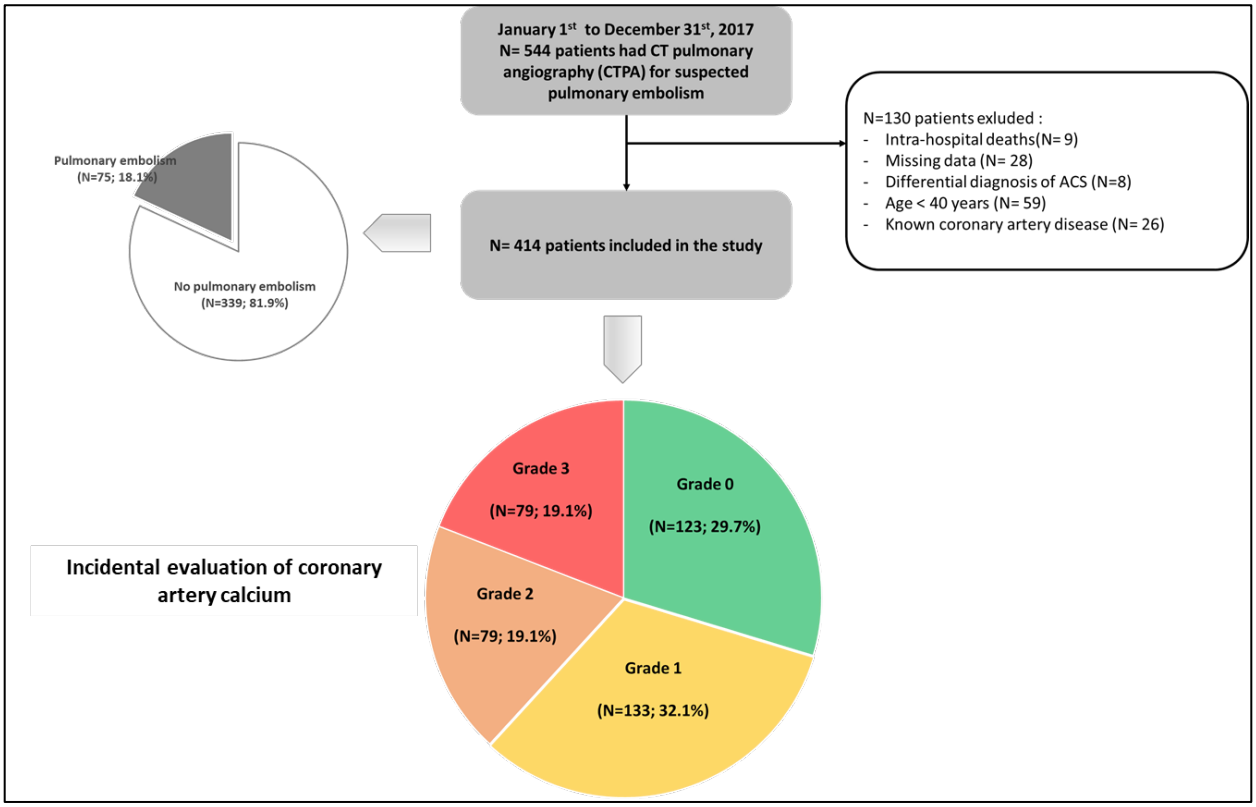
Event free survival during follow-up was evaluated according to the Kaplan-Meier method. The difference between subgroups was assessed using the log-rank test. Multivariate Cox regression was used to assess the predictive value of moderate to severe calcifications (grades 2 and 3) for the primary and secondary outcomes.

All analyses were done using SPSS version 21.0 (SPSS, Chicago, Illinois).

III. RESULTS

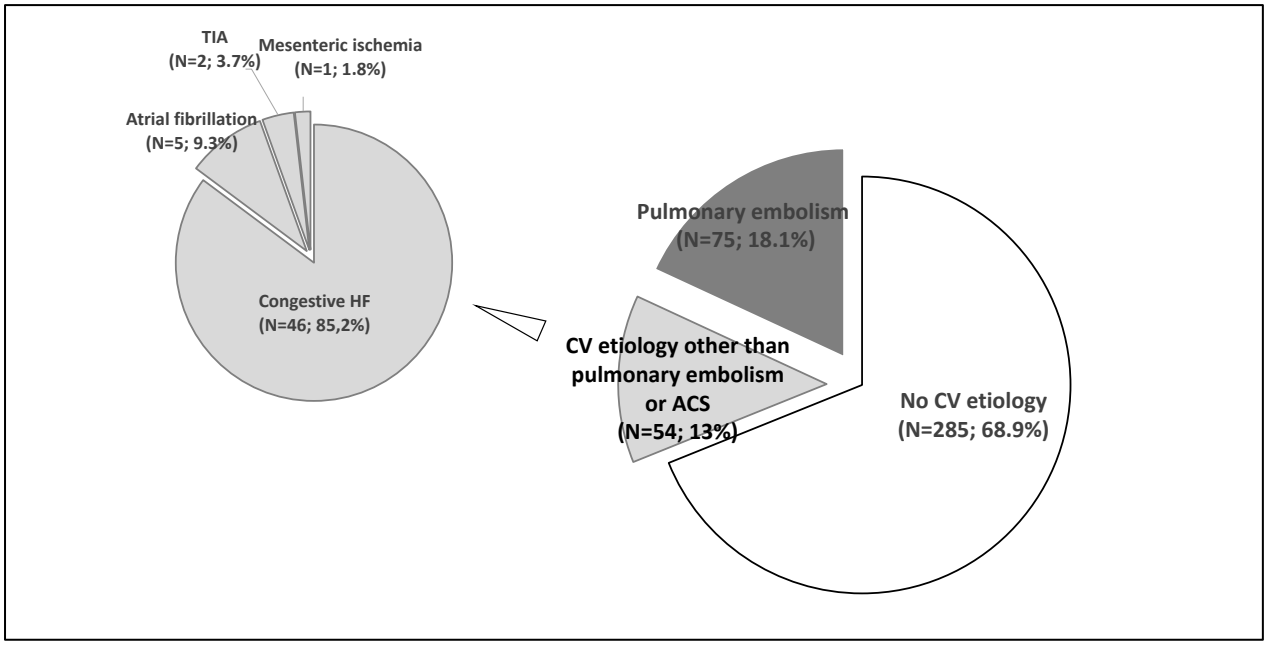
A total of 414 patients were included into the analysis (Figure 2 and Table 1). The mean age of our cohort was 69.7±14.3 years, and 42% were males. PE was diagnosed in 75 (18.1%) patients, and 54 additional patients (13%) had alternative cardiovascular events (Figure 3).

Figure 2. Study flow-chart and distribution of CAC categories



Abbreviations. CT=Computed tomography; CTPA=Computed tomography pulmonary angiography

Figure 3. Alternative CV etiologies in patients suspected for PE



Abbreviations: ACS=Acute coronary syndrome; CV=Cardiovascular; HF=Heart failure; PE=pulmonary embolism; TIA= Transient ischemic attack

III.1. Inter-observer agreement for incidental CAC evaluation

In PE patients, inter-observer agreement for CAC classification was excellent between senior radiologist and radiology resident (κ= 0.884, CI 95% 0.846-0.918; p<0.001) and substantial between senior radiologist and cardiology resident (κ=0.619, CI 95% 0.582-0.639; p<0.001). Regarding moderate to severe calcifications (grades 2 and 3) identification, inter-observer agreement was perfect (κ=1; p<0.001) and excellent between senior radiologist and cardiology resident (κ=0.802, CI 95% 0.789-0.818, p<0.001).

III.2. Distribution of CAC categories

The study population was subdivided according to incidental CAC evaluation as follows: grade 0 (N=123; 29.7%), grade 1 (N=133; 32.1%), grade 2 (N=79; 19.1%) and grade 3 (N=79; 19.1%). Table 1 presents the clinical characteristics of the four subgroups. More women had no calcification (grade 0) (p<0.001). Patients with moderate and severe calcifications (grades 2 and 3) were older, had higher prevalence of risk factors (hypertension, diabetes, dyslipidemia), chronic kidney disease (CKD) and prior stroke (all p<0.05). Aspirin and statins were more often prescribed in patients with grades 2-3 CAC (all p<0.05). No difference was found in CAC classification between PE and no PE patients (p=0.798). (Supplemental Figure 1)

Table 1. Baseline clinical characteristics of the study population

	All N= 414	Grade 0 N= 123	Grade 1 N= 133	Grade 2 N= 79	Grade 3 N= 79	P
Age, years, mean ± DS	69.7 ± 14.3	59.9 ± 12.9	69.8 ± 1.8	75.8 ±13.0	78.4 ± 10.3	**<0.001**
Males, n(%)	174 (42)	25 (20.3)	63 (47.4)	39 (49.4)	47 (59.5)	**<0.001**
Hypertension, n(%)	233 (56.4)	42 (34.1)	75 (56.4)	55 (69.6)	61 (78.2)	**<0.001**
Active or former smokers, n(%)	149 (36)	41 (33.4)	47 (35.3)	28 (35.5)	33 (42.3)	0.480
Dyslipidemia, n(%)	91 (22,0)	14 (11.4)	25 (18.8)	26 (329)	26 (33.3)	**<0.001**
Obesity, n(%)	89 (21,5)	26 (21.1)	32 (24.1)	12 (15.2)	19 (24.1)	0.441
Diabetes, n(%)	83 (20.0)	17 (13.8)	23 (17.3)	16 (20.3)	27 (34.2)	**0.004**
CKD (eGFR< 60ml/min), n(%)	99 (23.9)	19 (15.4)	27 (20.3)	23 (29.1)	30 (38)	**0.001**
PAD, n(%)	15 (3.6)	1 (0.8)	3 (2.3)	6 (7.6)	5 (6.3)	0.088
Prior stroke, n(%)	34 (8.3)	7 (5.7)	7 (5.3)	8 (10.1)	12 (15.4)	**0.042**
Prior cancer, n(%)	99 (24)	31 (25.2)	34 (25.6)	13 (16.5)	21 (26.9)	0.375
Baseline treatment						
Aspirin, n(%)	95 (23.1)	15 (12.2)	26 (19.5)	25 (31.6)	29 (37.7)	**<0.001**
Statin, n(%)	83 (20.1)	12 (9.8)	26 (19.5)	22 (27.8)	23 (29.5)	**0.001**

Abbreviations: CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; PAD=Peripheral artery disease.

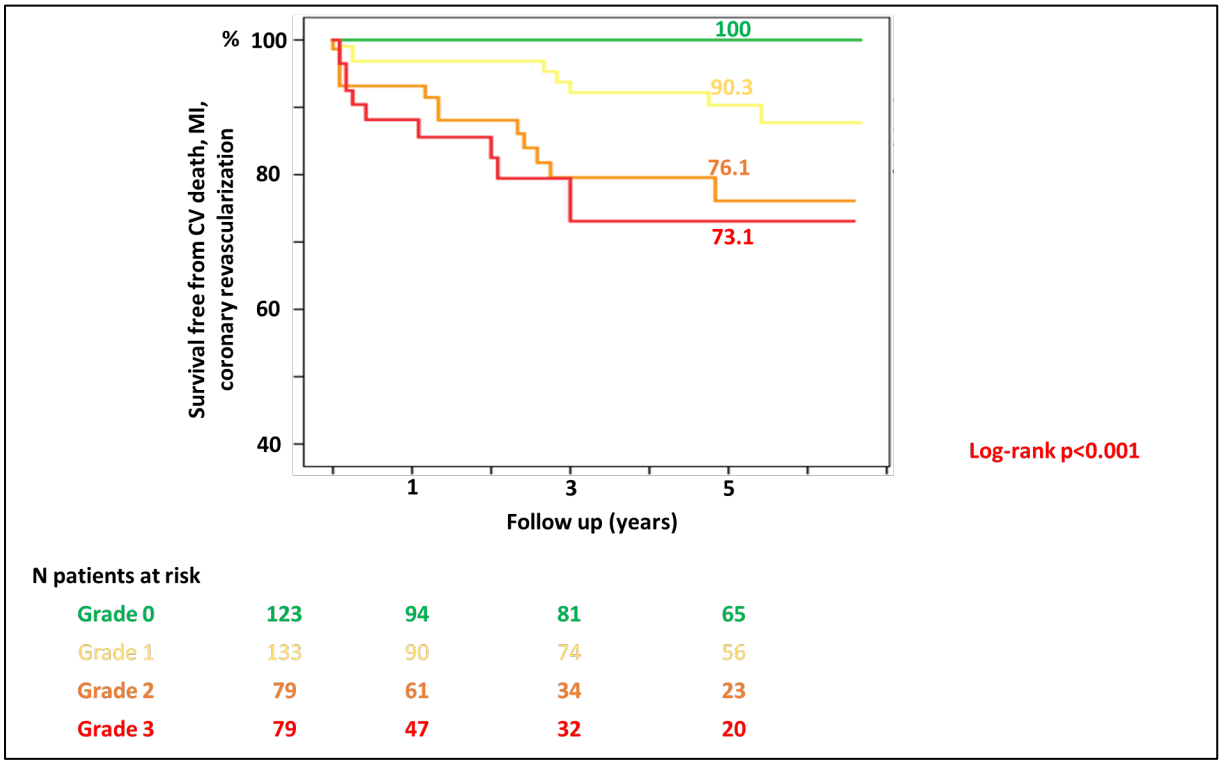
III.3. Cardiovascular outcomes

The mean follow-up was 3.5±2.4 years. Overall, 8.9% of patients experienced the primary composite outcome, while the rates of all-cause mortality and the secondary composite event were 41.3% and 20.5%, respectively.

Patients with CAC grades 2-3 had higher rates of primary composite outcome, all-cause mortality, and secondary composite event in comparison with those with grades 0-1 (all p<0.001) (Supplemental Table 1). Similar findings were in patients without PE (Supplemental Table 2). Whereas, in PE patients, only all-cause mortality was higher in grades 2-3 patients (p<0.019) (Supplemental Table 3).

During follow-up, none of the patients who had no CAC (grade 0) experienced any primary composite outcome. Five-year survival free from cardiovascular mortality, MI and coronary revascularization was significantly lower in patients with grades 2-3 CAC (76.1% and 73.1%, respectively) in comparison with those with grades 0 and 1 CAC (100% and 90.3%, respectively; p<0.001). Similar findings were observed in patients without PE (Supplemental Figure 2).

Figure 4. Kaplan-Meier curve of survival free from primary composite outcome



Abbreviations: CV=cardiovascular; MI= myocardial infarction

Patients with CAC grades 2-3 had higher all-cause mortality (survival at five years: 44.1% and 41.1%, respectively) and higher occurrence of the composite event (5-years event-free survival: 68.3% and 45.4%, respectively) as compared with those with grades 0 and 1 CAC ((76.3% and 59.5%; p<0.001) and (91.8% and 75.2%; p<0.001) respectively) (Figure 5 and 6). Similar findings were observed in patients without PE. (Supplemental Figures 3 and 4)

Figure 5. Kaplan-Meier curve of survival from all-cause mortality

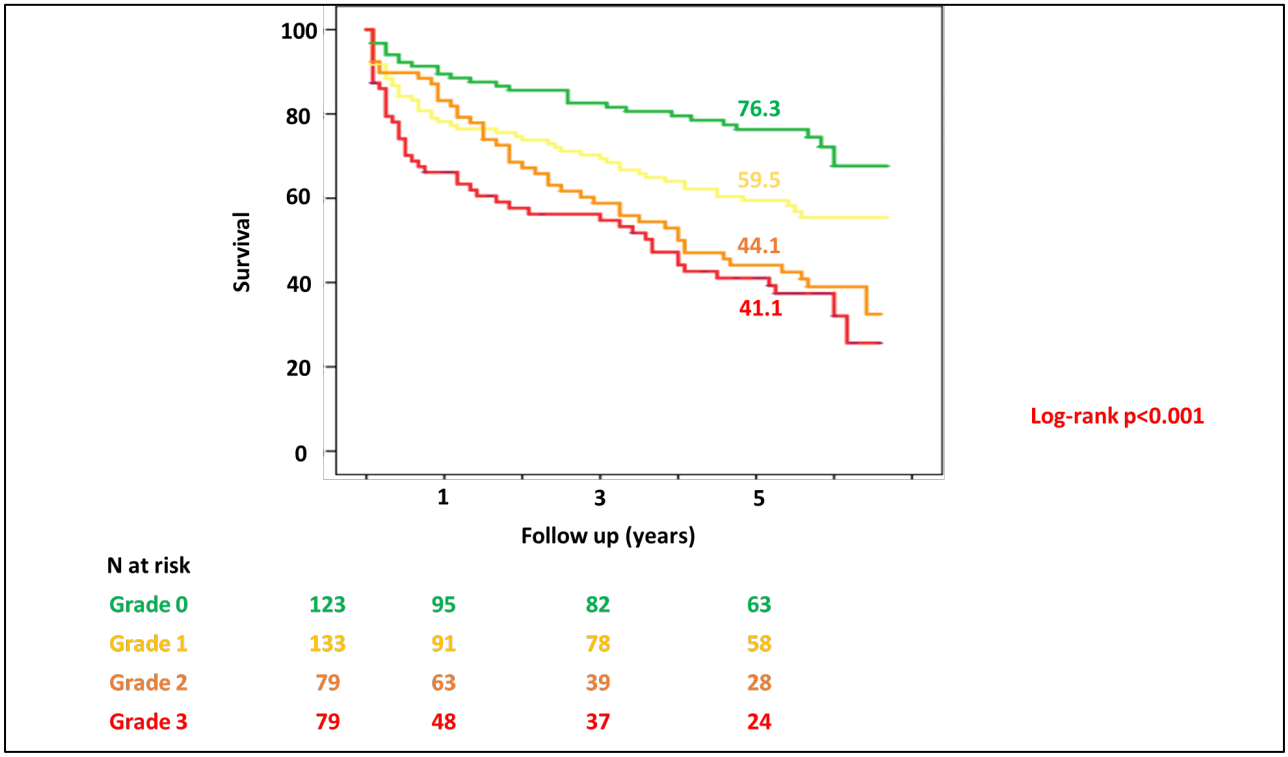
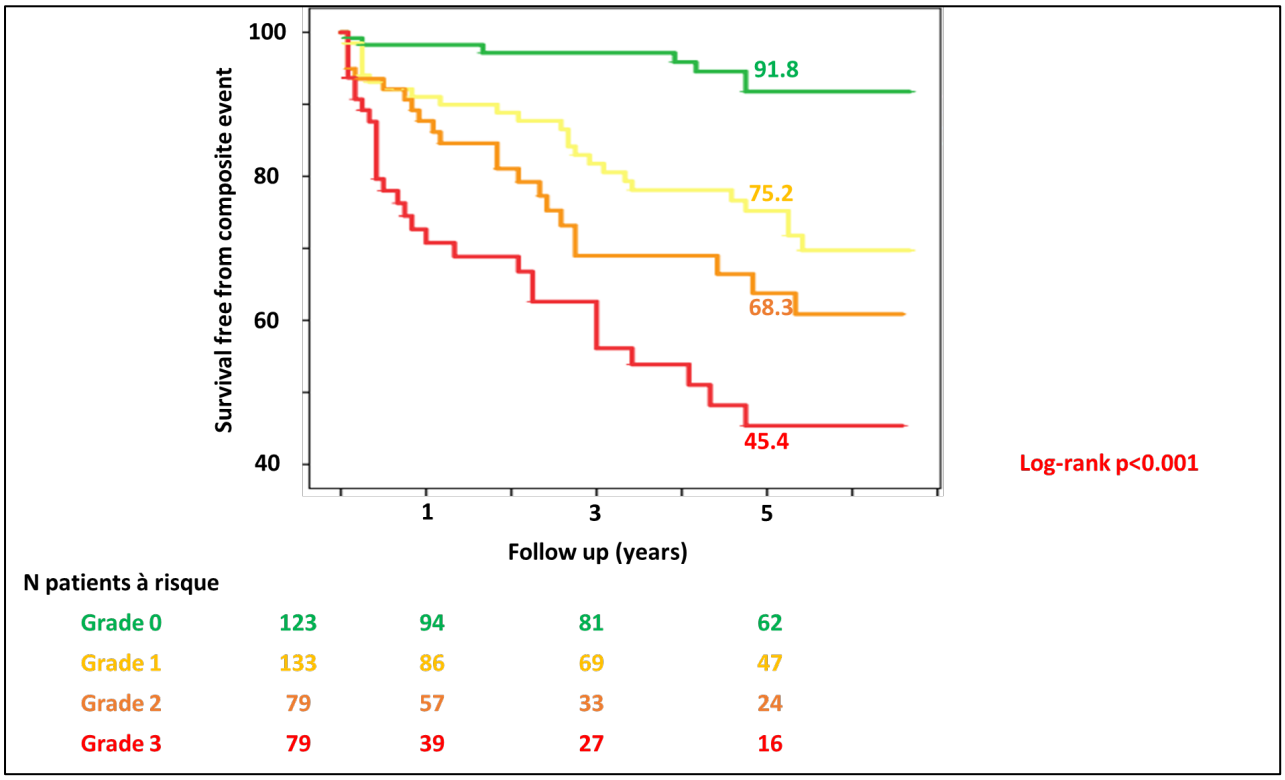


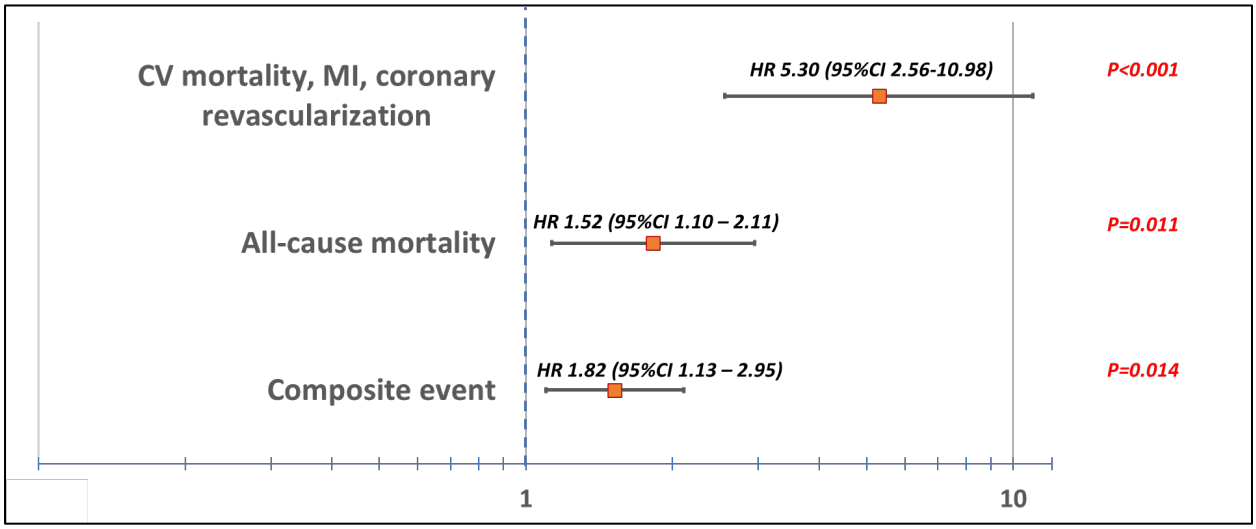
Figure 6. Kaplan-Meier curve of survival free from the composite event



III.4. Prognostic value of incidental CAC evaluation

After adjustment to age, sex, risk factors (hypertension, diabetes, dyslipidemia, smoking), peripheral artery disease, CKD and PE diagnosis, the presence of CAC grades 2-3 was independently associated with the primary outcome (HR=5.30, 95%CI 2.56-10.98; p<0.001), all-cause mortality (HR=1.52, 95%CI 1.10-2.11; p=0.011); and the extended composite event (HR=1.82, 95%CI 1.13-2.95; p=0.014) (Figure 7).

Figure 7. Forest plots - Prognostic value of moderate and severe CAC (grades 2 and 3)



**After adjustment to age, sex, risk factors (hypertension, diabetes, dyslipidemia, smoking), PAD, CKD and pulmonary embolism diagnosis*

Abbreviations: CAC=coronary artery calcification, CKD=chronic kidney disease, CV=cardiovascular; MI=Myocardial infarction, PAD: peripheral artery disease

IV. DISCUSSION

The major findings can be summarized as follows: i) the incidental visual CAC evaluation during CT for diagnosis of PE is a reproducible tool to estimate coronary atherosclerosis burden; ii) it could represent a valuable marker of cardiovascular risk in patients without known CAD; iii) CAC were present in 70.3% in patients who underwent CTPA for suspected PE; iv) In absence of CAC no patient experienced cardiovascular death, MI or coronary revascularization; v) Moderate and severe CAC (grades 2 and 3) were independent predictors of poorer mid-term cardiovascular prognosis.

IV.1. Incidental CAC visual assessment: a valuable and reproducible tool

While conventional Agatston scoring remains the gold-standard for CAC evaluation, it requires ECG-gates imaging, dedicated software and trained physicians.

Each year, millions of CT chest exams are performed for a variety of indications and may represent an opportunity to evaluate CAC despite being non-ECG-gated. Visual CAC scoring on thoracic CT scan represents an easy method for semi-quantitative assessment of the amount of CAC. The advantage of this visual score is that it can be used for both contrast-enhanced or non-contrast CT. In addition, it has also been shown that it correlated well with Agatston scoring. In a community based patient cohort who underwent routine non-contrast chest CT, Azour et al. demonstrated that visual ordinal scoring of CAC accurately predicted Agatston ranges ($r=0.811$ $p<0.01$)[5]. In the *National Lung Screening Trial*, overall CAC visual assessment exhibited good agreement with the categorized Agatston scores (weighted κ, 0.75), and the inter-observer agreement was good (mean κ of 0.85). In our study, inter-observer agreement was high between senior radiologist and radiology resident for CAC visual classification ($\kappa= 0.884$) and perfect for classifying grade 2/3 calcifications ($\kappa=1$). Similar finding was reported by Shao and coworkers[11]. Interestingly, although inter-observer agreement for CAC classification was only substantial between senior radiologist and cardiology resident, the agreement for moderate and severe CAC was excellent ($\kappa=0.802$). This suggests that visual CAC evaluation is a reproducible method that can be generalizable to real world practice even among physicians with limited training in cardiac imaging.

IV.2. Incidental visual CAC assessment: a marker of cardiovascular risk

In our cohort, patients with moderate and severe calcifications (grades 2 and 3) were older, more often males and had higher prevalence of cardiovascular risk factors. The MESA and Framingham studies[12,13] showed that the prevalence of CAC varies according to ethnicity, sex and age. Women are known to have less CAC than males counterparts[14]. The occurrence and severity of CAC were also both associated with traditional cardiovascular risk factors and cardiovascular risk scores[12,13]. Mamudu et al. showed that diabetes was associated with increased CAC (as assessed by Agatston method ≥400) and that CAC was increased in the presence of hypertension or hypercholesterolemia on top of diabetes[15]. As previously reported, we found that CKD is associated with increased CAC[16].

IV.3. Prognostic value of visual CAC categories

Shemesh et al. aimed to evaluate ordinal scoring of CAC on low-dose CT scan for lung cancer screening. At long-term follow-up, increasing CAC independently predicted cardiovascular deaths[17]. In the same setting, other reports using different incidental CAC evaluation methods have shown similar findings[6,18,19].

During the COVID-19 outbreak, chest CT scan was widely used for patients screening. Mousseaux et al. assessed the impact of incidental visual CAC estimation on 6-month mortality in COVID-19 patients. After adjustment moderate or severe CAC were associated with higher mortality (HR=2.26; p=0.03)[7].

In 479 patients with PE, Heidinger et al. found CAC in 52.8% of cases. Thirty-day mortality with severe (19.0%; OR 5.1 p = 0.011), moderate (11.2%; OR 2.7; p = 0.031), and mild CAC (12.6%; OR 3.1; p = 0.006) was higher than without CAC. PE-related mortality was also progressively increases with the severity of CAC (OR at 2.9, 4.0 and 5.8 for severe, moderate and mild CAC, respectively)[20].

Williams et al. investigated the impact of CAC (as assessed by modified Miller score, another semi quantitative non ECG-gated CAC scoring) on the 3-year prognosis of 400 patients with PE. The authors found that patients with CAC were three times more likely to die than patients without CAC and that severe CAC were the highest risk of 3-year mortality (HR 4.62; 95%CI 2.73-7.83 p<0.001)[21]. This impact of CAC was independent from PE severity[21].

In our cohort, after adjustments, moderate and severe (grades 2 and 3) CAC predicted independently, CV mortality, MI and coronary revascularization, all-cause mortality, and the extended composite cardiovascular event in patients who underwent a CTPA for suspected PE. The originality of our study was that we investigated all patients undergoing CTPA independently from PE diagnosis; the majority of our patients had no PE (81.9%). The prognostic impact of CAC was observed in all cohort as well as in patients without PE.

Importantly, neither coronary events (MI or coronary revascularization) nor cardiovascular mortality was observed in patients without CAC. Several studies confirmed the excellent negative predictive value in the absence of CAC[22,23]. Nonetheless, CAC zero does not exclude CAD and non-calcified plaques might be responsible for acute coronary events in high-risk asymptomatic patients[24].

IV.4. Perspectives and future directions

“Nothing is more expensive than a missed opportunity”[25] and this has become relevant for the reporting of incidental CAC as the important number of chest CT prescribed in various indications and the proven prognostic implications.

Incidental CAC could be considered as a tiebreaker for the decision to introduce and optimize the prescription of preventive medications (such as statins, aspirin). Of note, only one third of our patients with moderate and severe CAC were on aspirin and statin therapy.

In the *Incidental Coronary Calcification Quality Improvement Project* (NOTIFY-1) study, incidental CAC evaluation, along with physician and patient notification in the presence of CAC, was associated with a significantly greater prescription of lipid lowering therapy [26].

The randomized *Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research* (EISNER) trial assigned > 2,000 individuals to either undergo or not CAC scanning before risk factor counseling. At 4 years, subjects included in the CAC scoring arm showed an improvement in several cardiovascular risk factors (low-density lipoprotein-cholesterol (LDLc) level, systolic blood pressure, and weight) suggesting a better adherence of the patients to treatment prescription and counseling[27].

Automated assessment of CAC on chest CT using machine learning may improve the speed and accuracy of the radiologist reporting[28]. Peng et al, quantified CAC through a deep learning algorithm (DL-CAC) on non–ECG-gated chest CTs performed for routine care in all settings. After adjustment, patients with DL-CAC ≥100 had increased risk of death (HR: 1.51; 95% CI:1.28-1.79), all-cause mortality, MI, stroke (HR:1.57;95% CI:1.33-1.84), and all-cause mortality, MI, stroke, coronary revascularization (HR: 1.69; 95% CI: 1.45-1.98) compared with DL-CAC = 0 [29]. By using artificial intelligence (AI) DL algorithms, CAC can be quantified from non-gated CT chest scans without any supplementary cost or radiation to the patient. The pragmatic use of AI algorithms in reporting incidental CAC through “free” already available data has the potential to guide the prescription of prevention medications and motivate asymptomatic patients to make sustained lifestyle changes.

Finally, the absence of CAC in retrospective analysis of any previous non-ECG gated chest CT-scan could prevent the prescription of unnecessary coronary investigations with a CAC zero guarantee period of 3 and 5 years in asymptomatic patients with and without diabetes, respectively[30].

IV.5. Study limitations

The current study has some limitations. First, its retrospective, single-center design and relatively small samples size requires further confirmation. Second, PE severity was not assessed. Nonetheless, only a minority of patients (18.1%) were diagnosed with PE, and our point was rather to take the opportunity the CT scan to identify high-risk patients after elimination of PE diagnosis. Moreover, CAC location (which vessel, proximal or distal) was not detailed. Finally, the impact of incidental CAC evaluation on medical prescriptions of preventives therapies was beyond the scope of the current study.

V. CONCLUSION

In patients undergoing CTPA for suspicion for PE, CAC is frequently observed, and its semi-quantitative estimation represents a simple, reproducible, cost-free and valuable marker of cardiovascular risk that can be useful even for non-cardiac-imaging specialists. Incidental assessment of CAC in different clinical settings requiring chest CT exams could provide important information regarding long-term cardiovascular outcomes and guide tailored preventive strategies. In the future, artificial intelligence DL algorithms could enhance the systematic reporting of CAC evaluation and generalize its use in clinical practice.

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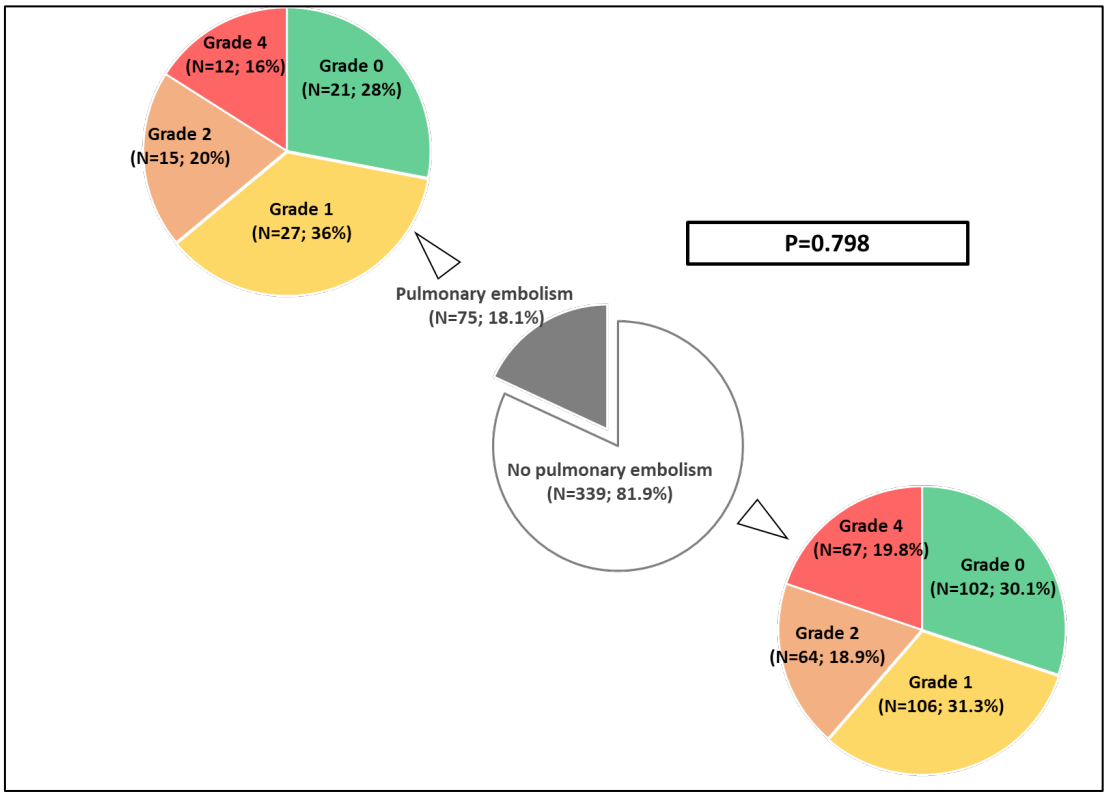
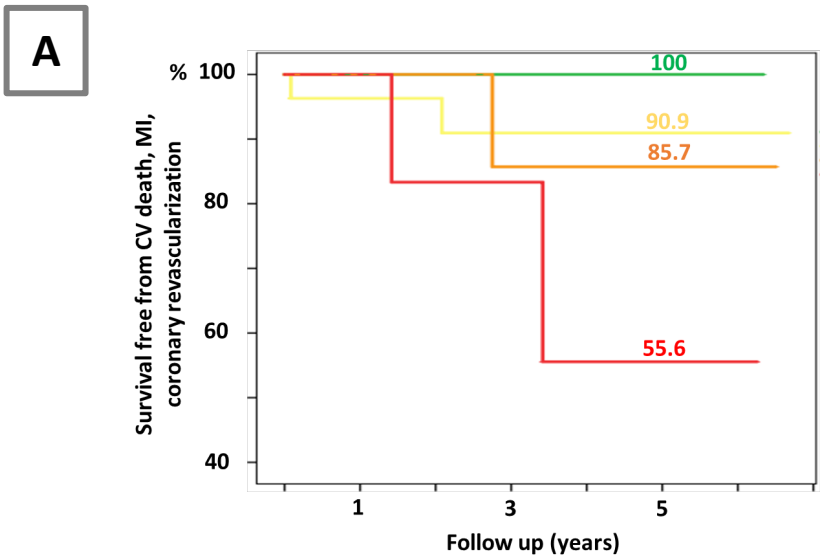
Annexes

Supplemental figure 1. Incidental CAC visual assessment in patients with and without pulmonary embolism

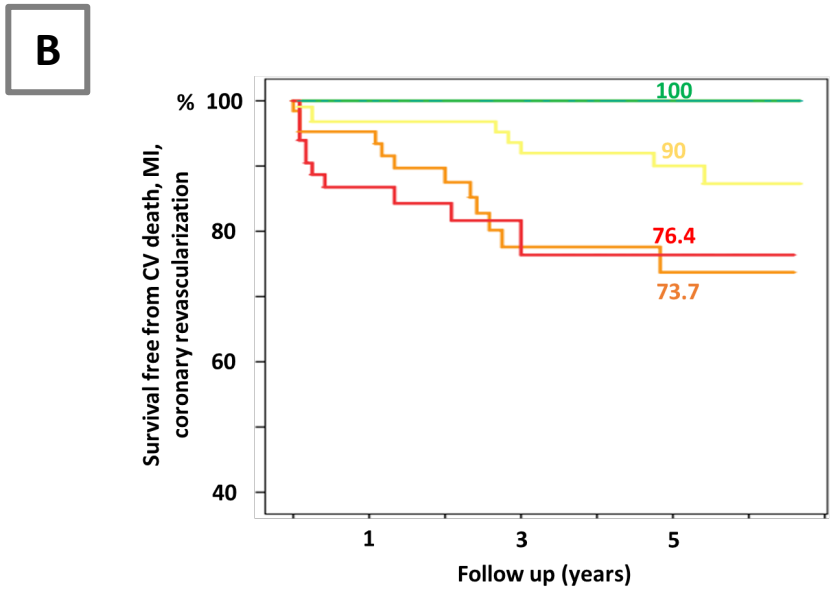


Supplemental figure 2. Kaplan-Meier curve of survival free from primary composite outcome in patients with (A) and without (B) pulmonary embolism



N patients at risk

Grade 0	21	15	13	11
Grade 1	27	19	17	14
Grade 2	15	10	7	6
Grade 3	12	9	3	1



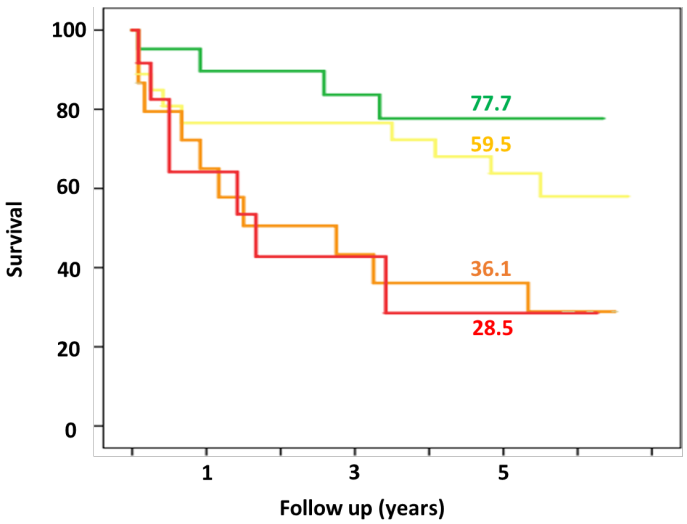
N patients at risk

Grade 0	102	79	68	54
Grade 1	106	71	57	42
Grade 2	64	51	27	17
Grade 3	67	38	29	19

Abbreviations: CV=cardiovascular

Supplemental figure 3. Kaplan-Meier curve of survival free from all-cause mortality in patients with (A) and without (B) pulmonary embolism

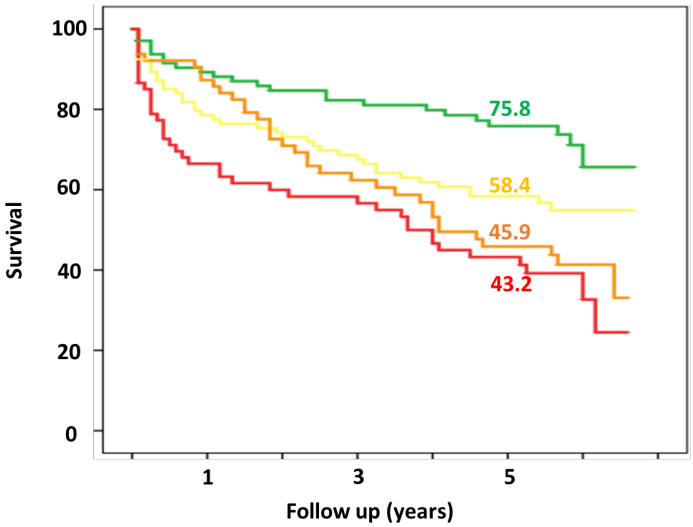
A



Log-rank p=0.010

N at risk				
Grade 0	21	15	13	9
Grade 1	27	18	18	12
Grade 2	15	9	6	5
Grade 3	12	9	3	1

B

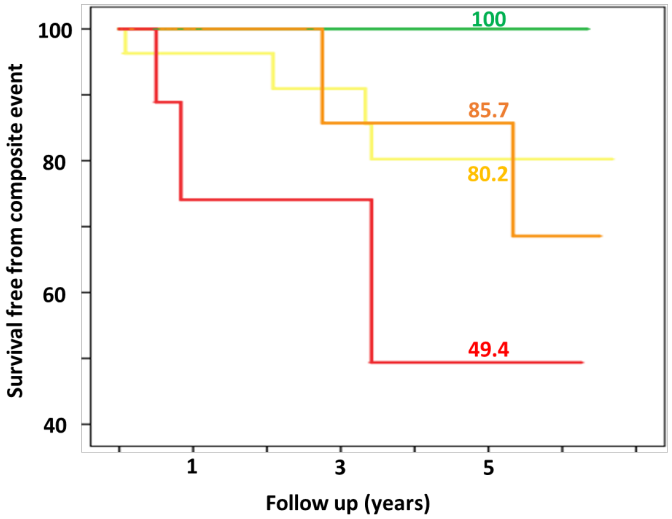


Log-rank p<0.001

N at risk				
Grade 0	102	79	68	54
Grade 1	106	73	60	46
Grade 2	64	54	34	23
Grade 3	67	42	34	23

Supplemental figure 4. Kaplan-Meier curve of survival free from the composite event in patients with (A) and without (B) pulmonary embolism

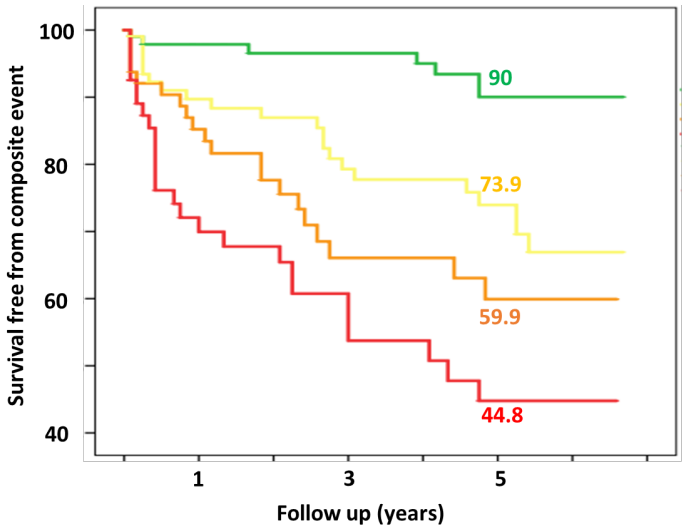
A



Log-rank p=0.037

N at risk				
Grade 0	21	16	14	11
Grade 1	27	18	17	10
Grade 2	15	9	6	5
Grade 3	12	5	3	1

B



Log-rank p<0.001

N at risk				
Grade 0	102	78	66	51
Grade 1	106	67	51	36
Grade 2	64	48	26	18
Grade 3	67	33	23	13

Supplemental table 1. Cardiovascular outcomes

	All (N= 414)	Grade 0 (N=123)	Grade 1 (N=133)	Grade 2 (N=79)	Grade 3 (N=79)	P
All-cause mortality	171 (41.3)	28 (22.8)	51 (38.5)	45 (57)	47 (59.5)	**<0.001**
Cardiovascular mortality, n(%)	19 (4.6)	0	5 (3.8)	5 (6.3)	9 (11.4)	**0.002**
MI, n(%)	8 (1.9)	0	1 (0.8)	4 (5.1)	3 (3.8)	**0.030**
Coronary revascularization, n(%)	16 (3.9)	0	4 (3.0)	8 (10.1)	4 (5.1)	**0,003**
Cardiovascular mortality, MI, coronary revascularization, n(%)	37 (8.9)	0	10 (7.6)	13 (16.5)	14 (17.7)	**<0.001**
Ischemic stroke, n(%)	20 (4.8)	4 (3.3)	7 (5.3)	3 (3.8)	6 (7.6)	0.529
Ischemic peripheral event, n(%)	15 (3.6)	1 (0.8)	5 (3.8)	2 (2.5)	7 (8.9)	**0.026**
Hospitalization for HF, n(%)	35 (8.5)	3 (2.4)	11 (8.3)	9 (11.4)	12 (15.2)	**0.010**
Composite event, n(%)	85 (20.5)	7 (5.7)	36 (19.5)	22 (27.8)	30 (38)	**<0.001**

Abbreviations: HF=Heart failure; MI=Myocardial infarction

Supplemental table 2. Cardiovascular outcomes in patients without pulmonary embolism

	No PE (N= 339)	Grade 0 (N=102)	Grade 1 (N=106)	Grade 2 (N=64)	Grade 3 (N=67)	P
All-cause mortality	140 (41.3)	24 (23.5)	41 (38.7)	35 (54.7)	40 (59.7)	**<0.001**
Cardiovascular mortality, n(%)	15 (4.4)	0	4 (3.8)	4 (6.3)	7 (10.4)	**0.011**
MI, n(%)	7 (2.1)	0	0	4 (6.3)	3 (4.5)	**0.008**
Coronary revascularization, n(%)	16 (4.7)	0	4 (3.8)	8 (12.5)	4 (6)	**0.003**
Cardiovascular mortality, MI, coronary revascularization,n(%)	32 (9.4)	0	8 (7.5)	12 (18.8)	12 (17.9)	**<0.001**
Ischemic stroke, n(%)	19 (5.6)	4 (3.9)	6 (5.7)	3 (4.7)	6 (9)	0.558
Ischemic peripheral event, n(%)	15 (4.4)	1 (1)	5 (4.7)	2 (3.1)	7 (10.4)	**0.031**
Hospitalization for HF, n(%)	31 (9.1)	3 (2.4)	10 (9.4)	8 (12.5)	10 (14.9)	**0.040**
Composite event, n(%)	76 (22.4)	7 (9.2)	22 (28.9)	20 (26.3)	27 (35.5)	**<0.001**

Abbreviations: HF=Heart failure; MI=Myocardial infarction

Supplemental table 3. Cardiovascular outcomes in patients with pulmonary embolism

	PE (N= 75)	Grade 0 (N=21)	Grade 1 (N=27)	Grade 2 (N=15)	Grade 3 (N=12)	P
All-cause mortality	31 (41.3)	4 (19)	10 (37)	10 (66.7)	7 (58.3)	**0.019**
Cardiovascular mortality, n(%)	4 (5.3)	0	1 (3.7)	1 (6.7)	2 (16.7)	0.219
MI, n(%)	1 (1.3)	0	1 (3.7)	0	0	0.615
Coronary revascularization, n(%)	0	0	0	0	0	-
Cardiovascular mortality, MI, coronary revascularization, n(%)	5 (6.7)	0	2 (7.4)	1 (6.7)	2 (16.7)	0.327
Ischemic stroke, n(%)	1 (1.3)	0	1 (3.7)	0	0	0.615
Ischemic peripheral event, n(%)	0	0	0	0	0	-
Hospitalization for HF, n(%)	4 (5.3)	0	1 (3.7)	1 (6.7)	2 (16.7)	0.219
Composite event, n(%)	9 (12)	0	4 (14.9)	2 (13.3)	3 (25)	0.171

Abbreviations: HF=Heart failure; MI=Myocardial infarction

Serment d’Hippocrate

En présence des maîtres de cette école, de mes condisciples, je promets et je jure d’être fidèle aux lois de l’honneur et de la probité dans l’exercice de la médecine.

Je dispenserai mes soins sans distinction de race, de religion, d’idéologie ou de situation sociale.

Admis à l’intérieur des maisons, mes yeux ne verront pas ce qui s’y passe, ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser les crimes.

Je serai reconnaissant envers mes maîtres, et solidaire moralement de mes confrères. Conscient de mes responsabilités envers les patients, je continuerai à perfectionner mon savoir.

Si je remplis ce serment sans l’enfreindre, qu’il me soit donné de jouir de l’estime des hommes et de mes condisciples, si je le viole et que je me parjure, puissé-je avoir un sort contraire.

Valeur pronostique de la description d'un score calcique visuel sur des angioscanners pulmonaires réalisés pour suspicion d'embolie pulmonaire

Introduction : L'imagerie par scanner est une méthode non-invasive pour identifier les calcifications des artères coronaire (CAC) qui représentent un marqueur d'athérosclérose et un facteur prédictif d'événements cardiaques chez les patients asymptomatiques.
Objectif : Investiguer l'association entre l'évaluation visuelle des calcifications coronaires sur des angioscanners pulmonaires (AP) et la survenue d'évènement cardiovasculaires chez les patients suspects d'embolie pulmonaire (EP) sans antécédent de maladie coronaire
Méthodes : Il s'agit d'une étude rétrospective monocentrique incluant des patients ayant eu un AP pour suspicion d'EP. Les patients ont été classés en quatre groupes en fonction de l'étendue et de la gravité des CAC : aucune (grade 0), légères (grade 1), modérées (grade 2) et sévères (grade 3). Le critère de jugement primaire était un composite de mortalité cardiovasculaire, d'infarctus du myocarde (IDM) ou de revascularisation coronarienne. Les critères de jugement secondaires étaient la mortalité toutes causes confondues et un évènement composite comprenant la mortalité cardiovasculaire, l'IDM, la revascularisation coronaire, l'accident vasculaire cérébral ischémique, les événements périphériques ischémiques et l'hospitalisation pour insuffisance cardiaque.
Résultats : Au total, 414 patients (âge moyen 69,7±14,3 ans, 42 % d'hommes, 18,1 % EP) ont été inclus répartis selon les CAC comme suit : grade 0 (N=123; 29,7 %), grade 1 (N=133; 32,1 %), grade 2 (N=79; 19,1 %) et grade 3 (N=79 ; 29,7 %). Le suivi moyen était de 3,5±2,4 ans. Après ajustement, la présence de CAC grades 2-3 prédisait indépendamment le critère de jugement primaire composite (HR = 5,30, IC95% 2,56-10,98; p<0,001). La présence de CAC de grades 2-3 était également indépendamment prédictive de mortalité toutes causes (HR=1,52, IC95 % 1,10-2,11; p=0,011); et l'événement composite (HR = 1,82, IC95 % 1,13-2,95 ; p = 0,014).
Conclusion : L'évaluation visuelle du CAC lors des AP pourrait avoir une valeur pronostique cardiovasculaire à moyen terme indépendamment du diagnostic d'EP.

Mots-clés : Calcifications coronaires ; angioscanner pulmonaire, pronostic cardiovasculaire

Prognostic value of incidental coronary calcium in CT pulmonary angiography for suspected pulmonary embolism

Background: Computed tomography (CT) has emerged as a non-invasive method to identify directly coronary artery calcifications (CAC), a marker of atherosclerosis, and an independent predictor for major cardiac events in asymptomatic patients.
Aim: We sought to investigate the association between incidental visual CAC evaluation in CT pulmonary angiography (CTPA) for pulmonary embolism (PE) suspicion and the occurrence of cardiovascular events in patients without known coronary artery disease (CAD).
Methods: This was a retrospective single center study including patients who underwent CTPA for suspected PE. Patients were categorized in four groups according to the extent and severity of CAC: none (grade 0), mild (grade 1), moderate (grade 2) and severe (grade 3). The primary outcome was a composite of cardiovascular mortality, myocardial infarction (MI) or coronary revascularization. The secondary outcomes were all-cause mortality, and an extended composite outcome including cardiovascular mortality, MI, coronary revascularization, ischemic stroke, ischemic peripheral events and hospitalization for heart failure.
Results: A total of 414 patients (mean age 69.7 ± 14.3 years, 42% males, 18.1% PE) were included into the analysis and subdivided according to CAC categories as follows: grade 0 (N=123; 29.7%), grade 1 (N=133; 32.1%), grade 2 (N=79; 19.1%) and grade 3 (N=79;19.1%). The mean follow-up was 3.5±2.4 years. After adjustment, the presence of CAC grades 2-3 CAC predicted independently the primary outcome (HR=5.30, 95%CI 2.56-10.98; p<0.001). CAC grades 2-3 were also independent predictors for all-cause mortality (HR=1.52, 95%CI 1.10-2.11; p=0.011); and the extended composite event (HR=1.82, 95%CI 1.13-2.95; p=0.014).
Conclusion: In patients undergoing CT for suspicion of PE, the opportunistic assessment of CAC could provide important mid-term prognostic information, independently from the PE findings.

Keywords : coronary artery calcification; CT pulmonary angiography; cardiovascular outcome