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CARDIAC

# Extracardiac findings on coronary computed tomography angiography in patients without significant coronary artery disease

Philipp Karius [1] · Alexander Lembcke [1] · Felix C. Sokolowski [1] · Ivan Dario Perez Gandara [1] · Alejandra Rodríguez [1] · Bernd Hamm [1] · Marc Dewey [1]

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## Abstract

**Objective** To analyse extracardiac findings in patients without significant coronary artery disease (CAD) in general and in symptomatic patients in particular.

**Methods** We searched the Radiology Information System database for coronary computed tomography angiographies (CTA) performed from 2000–2014 and retrospectively enrolled 3,898 patients without significant CAD (coronary stenosis < 50%) in CTA. In 2,330 symptomatic patients, we analysed the spectrum of extracardiac findings and identified pathologies potentially explaining chest pain. Finally, we investigated variables affecting the number of extracardiac findings detected in CTA.

**Results** Overall extracardiac findings were found in 1,177 patients (30.2%; 95%CI, 28.8–31.7%). 94 patients (2.4%; 95%CI, 2.0–2.9%) had extracardiac findings with a recommendation for follow-up, sixteen patients (0.4%; 95%CI, 0.3–0.7%) had incidental urgent, and another three patients (0.1%; 95%CI, 0.1–0.2%) had incidental malignant extracardiac findings. 185 of 2,330 symptomatic patients (7.9%; 95%CI, 6.9–9.1%) revealed extracardiac findings potentially explaining chest pain after exclusion of significant CAD. The number of extracardiac findings increased significantly with patient age ($p < 0.001$) and the cumulative experience of the CT reader ($p < 0.001$).

**Conclusion** 30.2% of patients undergoing CTA for exclusion of CAD had ECF, and 7.9% of symptomatic patients without significant CAD on their examination had findings that could potentially explain their symptoms.

**Key Points**

- *Of patients undergoing CTA, 2.8% have relevant incidental extracardiac findings.*
- *CTA could identify the differential diagnosis of chest pain when excluding significant CAD.*
- *Patient age and reader's professional experience influence the number of detected ECFs.*

**Keywords** Tomography, x-ray computed · Coronary angiography · Incidental findings · Chest pain · Angina pectoris

**Abbreviations**

| | |
|---|---|
| CAD | Coronary artery disease |
| CTA | Coronary computed tomography angiography |
| ECF | Extracardiac finding |
| ECG | Electrocardiogram |
| FOV | Field of view |
| MDCT | Multiple-detector computed tomography |
| NCCP | Noncardiac chest pain |
| PET | Positron emission tomography |
| RIS | Radiology Information System |
| SPECT | Single-photon emission computed tomography |

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✉ Marc Dewey
dewey@charite.de

[1] Charite Medical School, Humboldt-Universität zu Berlin, Freie Universitat Berlin, Chariteplatz 1, 10117 Berlin, Germany

## Introduction

ECG-gated contrast-enhanced computed tomography angiography (CTA) is a well-established noninvasive imaging modality for the evaluation of cardiac structures in general and coronary arteries in particular. Scanner evolution has improved spatial and temporal resolution while lowering radiation exposure [1]. Due to its high negative predictive value, CTA is recommended to rule out coronary artery disease (CAD) in patients with a low to intermediate risk of disease [2, 3]. Consequently, CAD is excluded in most of these patients, leaving physicians with the task of performing additional diagnostic tests to identify the cause of the patients' initial symptoms [4, 5]. Unlike invasive coronary angiography (ICA), CTA additionally allows evaluations of structures outside the heart, thus providing a broader diagnostic approach and offering the opportunity to detect clinically relevant pathology or to identify alternative underlying causes in patients without CAD but persistent chest pain. Approximately half of all patients presenting with angina-like symptoms are diagnosed with atypical chest pain [6]. Tevalla et al found 33% of patients presenting with chest pain and undergoing coronary angiography to have insignificant CAD (coronary stenosis < 50%). Half of them have persistent chest pain after 12 months, pointing to a noncoronary (i.e., valvular heart disease, pericarditis or cardiomyopathy) or even extracardiac underlying etiology [7]. Pulmonary embolism, aortic dissection, tension pneumothorax, pulmonary infection, pulmonary effusion, and hiatal hernia are the most important extracardiac differential diagnoses causing noncardiac chest pain (NCCP) [5–7]. Kienzle et al additionally identified musculoskeletal and psychogenic causes of NCCP [8]. Thus, in patients with persistent symptoms, standard diagnostic workup including troponin testing, ECG, and ICA potentially misses important diagnoses, leading to inadequate patient management and a need for additional tests [6].

Nevertheless, reading CTA for extracardiac findings (ECFs) is discussed controversially. Some scientists appreciate the extended diagnostic value of CTA [5, 9, 10]. Since CTA allows large field of view (FOV) reconstruction from the raw data, it seems to be mandatory for radiologists to also have a look at adjacent anatomical structures in order not to miss important findings [5]. Others worry about the initiation of further diagnostic imaging without proven benefit, leading to additional radiation exposure and costs [11, 12]. Suspicious pulmonary nodules are the most frequently detected ECFs [11–13]. However, the results of the National Screening Lung Cancer Trial (NSLT) indicate that 96.4% of such pulmonary nodules ultimately turn out to be benign [14].

Since CTA is expected to rule out CAD in the vast majority of patients we suppose that reading CT images for extracardiac pathologies reveals relevant information in the interest of patients' health, in particular for those with insignificant CAD but persistent chest pain. Our primary aim was to describe and to quantify the spectrum of overall ECFs in CTA. Second, our goal was to identify incidental relevant ECFs leading to a change in further diagnostic or therapeutic management. Third, we sought to identify those ECFs that could explain chest pain in symptomatic patients in the same CTA examination that rules out significant CAD. Finally, we investigated variables influencing the detection of ECFs.

## Materials and methods

### Data sources and search

We performed a retrospective study at the Department of Radiology at Charité-Universitätsmedizin Berlin on 7 October 2016 and searched the Radiology Information System (RIS) for all cardiac CTs performed from 2000 until September 2014. This search retrieved a total data set of 10,017 cardiac CTs. To retrieve a maximum of relevant data, we determined an observational period of at least 2 years for each ECFs for which follow-up was recommended. Therefore, follow-up results were extracted from the electronic patient files until 7 February 2017. The Charité's ethics committee approved this retrospective study on 19 September 2016.

### Inclusion and exclusion criteria

We included all CTA examinations performed with the indication to rule out CAD. CTAs diagnosing significant CAD (coronary stenosis > 50%) were excluded as were CTAs with inadequate reports. Extremely abridged CTA reports just briefly describing the coronary status and not mentioning extracardiac structures were classified as inadequate for further analysis.

### Assessment of ECFs

An ECF was defined as an abnormality outside the heart and pericardium. Overall ECFs included both previously known and new incidental pathologies. Relevant incidental ECFs included ECFs with a recommendation for follow-up, urgent ECFs, and malignant ECFs previously unknown from the patient's history. ECFs with a recommendation for follow-up required additional investigation to confirm the diagnosis regarding characterisation (benign versus malignant) or entity. An ECF was classified as urgent when prompt therapy was recommended by the radiologist. Recommendations were issued at the time of the scan. ECFs were assigned to anatomical structures and—if possible—to organs or groups of pathologies for subclass analysis. For the purpose of this study, we defined a pulmonary nodule as a solid, subsolid, or calcified spheroid opacity of any size. A thoracic aorta exceeding a maximum diameter of 40 mm was categorised as a dilated aorta, while a dilatation over 50 mm was classified as aortic aneurysm.

### Data extraction and statistical analysis

Statistical analysis was performed for overall ECFs and relevant ECFs. Furthermore, patients with chest pain were identified to describe the spectrum of ECFs potentially explaining symptoms in patients without significant CAD largely following the concept of Kienzl et al [8]. We calculated prevalences and 95%

confidence intervals (CI) for overall and relevant ECFs as well as for ECFs that potentially explained chest pain. Given that very low proportions were found in the analysis, the confidence intervals were calculated using Wilson's formula. These confidence intervals show a better coverage than others based on normal approximations [15]. Statistical analysis was run on a per-patient basis. Furthermore, we documented all available follow-up examinations that were necessary to clarify the diagnosis. We also assessed temporal trends in average numbers of ECFs per CTA over the study period. To this end, we estimated a Poisson regression on the number of ECFs, assuming independence of findings within one examined image, and related these probabilities to patient gender and age, the volume of contrast medium, as well as the number of CT readers and their cumulative professional experience measured by years of professional activity in radiology. We considered the explanatory capacity of each covariate for the probability of finding a higher number of ECFs. Backward stepwise selection methods based on the improvement of fit (AIC criteria) were used to establish which of the five covariates included in the models had the highest explanatory power. Relevant data for temporal trend and multivariate analysis were primarily extracted from our RIS. Missing data were added from the technical sections of CTA reports and from the electronic patient file. Finally, multivariate analysis was performed on the basis of 3788 complete data sets of CTA examinations, representing 90.0% of all CTAs in our study population. Most cases of missing data occurred in the first 3 years of the total study period. Due to insufficient numbers of complete data sets guaranteeing statistical independence, CTAs of 2000 ($n = 1$) and 2002 ($n = 1$) were not taken into account when calculating the annualised average ECF. Data extraction from the original CTA reports and analysis were performed by Philipp Karius and Felix C. Sokolowski according to the STROBE guideline [16]. Statistical calculation was done by Alejandra Rodríguez and Ivan Dario Perez Gandara using R version 3.4.1 and R Studio version 1.0.153. Unclear cases were jointly solved in consensus with Marc Dewey.

## CTA

The CTs included in our retrospective analysis were performed as ECG-gated coronary CT angiography. Altogether, 96 radiologists were involved in reading the included CTAs; 17.1% of the CTAs were assessed by two readers. Information on the CT scanners used during the study period is compiled in ESM Table 1.

# Results

## CTA report selection and study cohort

A total of 10,017 CTAs were extracted from RIS, among them 5056 CTAs that were performed with the indication to rule out CAD. A diagnosis of significant CAD was made in 820 CTAs (16.2%), which were excluded. After eliminating 27 CTAs with inadequate reports, 4209 CTAs performed in 3898

**Table 1** Overall extracardiac findings in CTA by frequency

| ECFs | *N* | Prevalence | 95% CI | Cumulative frequency |
|---|---|---|---|---|
| Chronic changes of lung parenchyma and bronchial system | 501 | 12.9% | 11.8–13.9% | 29.6% |
| Extensive atherosclerosis | 209 | 5.4% | 4.7–6.1% | 42.0% |
| Pulmonary nodule/consolidation | 167 | 4.3% | 3.7–5.0% | 51.8% |
| Extensive spinal degeneration | 159 | 4.1% | 3.5–4.7% | 61.2% |
| Aortic dilatation | 112 | 2.9% | 2.4–3.4% | 68.1% |
| Enlarged/calcified lymph node | 107 | 2.7% | 2.3–3.3% | 74.4% |
| Hiatal hernia | 94 | 2.4% | 2.0–2.9% | 80.0% |
| Liver mass/(cystic) lesion | 61 | 1.6% | 1.2–2.0% | 83.6% |
| Pleural lesion | 53 | 1.4% | 1.0–1.8% | 86.8% |
| Vascular anomaly | 21 | 0.5% | 0.4–0.8% | 88.0% |
| Pleural effusion | 20 | 0.5% | 0.3–0.8% | 89.2% |
| Diaphragmatic elevation | 14 | 0.4% | 0.2–0.6% | 90.0% |
| Other ECFs | 165 | 4.2% | 3.6–4.9% | 100.0% |
| No. of ECFs | 1,683 | | | |
| No. of patients with ECFs [a] | 1,177 | | | |
| No. of patients in study cohort | 3,898 | | | |
| Prevalence of ECFs [b] | | 30.2% | 28.8–31.7% | |

[a] 364 patients had more than one ECF

[b] No. of patients with ECFs related to no. of patients in study cohort

patients that ruled out CAD remained for further analysis (Fig. 1). The final study population had a mean age of 59.1 ± 12.4 years and a 50.6% proportion of female patients.

## Overall ECFs

Overall, ECFs were identified in 1177 patients, corresponding to a prevalence of 30.2% (95% CI, 28.8–31.7%) (Table 1). ECFs affecting the lungs and pleura were most common (45.4%; 95% CI, 43.0–47.8%), followed by vascular ECFs (22.5%; 95% CI, 20.6–24.6%), ECFs of the upper abdomen (12.1%; 95% CI, 10.6–13.8%), skeletal ECFs (11.4%; 95% CI, 10.0–13.0%), and mediastinal ECFs (7.6%; 95% CI, 6.4–9.0%) (Fig. 2). Detailed results on overall ECFs are given in ESM Table 2.

Ranked by frequency, 90% of all ECFs were accounted for by chronic pulmonary changes, extensive atherosclerosis, pulmonary nodules, spinal degeneration, aortic dilation, enlarged/calcified lymph nodes, hiatal hernias, liver lesions, pleural lesions, aortic aneurysms, other nonaortic vascular anomalies, pleural effusion, and diaphragmatic elevation (Table 1).

## Relevant ECF

### Incidental ECFs with recommendation for follow-up

A total of 2.4% of patients (95% CI, 2.0–2.9%) (94 patients) had ECFs with a recommendation for follow-up. More than three quarters of them had suspicious pulmonary nodules, liver lesions, or chronic changes of the lung parenchyma and bronchial system. Two patients had two ECFs with a need for further evaluation (Table 2). The mean observation period for ECFs with a recommendation for follow-up was 5.0 ± 2.6 years. Follow-up data were available from the SAP electronic patient files in 30 of 95 patients (31.6%). Among those, further investigation led to relevant findings affecting further treatment in four cases. Two patients were finally diagnosed with bronchial cancer (malignant ECF) by PET-CT and bronchoscopy. One patient each had sarcoidosis and infectious consolidation (urgent ECF). The remaining follow-ups revealed nonspecific abnormalities.

### Incidental urgent ECF

Of patients, 0.4% (95% CI, 0.3–0.7%) (16 patients) had urgent incidental ECFs. Ten patients were diagnosed with incidental pulmonary embolism, among them one patient with concomitant massive pleural effusion. Five patients had pulmonary infection, and another patient was diagnosed with sarcoidosis (Table 2). Three of the patients with pulmonary embolism suffered from previously known renal cell carcinoma.

### Incidental malignant ECF

Incidental malignant ECFs were found in 0.1% (95% CI, 0.0 – 0.2%) (3 patients) of the study cohort. Bronchial cancer was finally diagnosed in two patients during follow-up and another

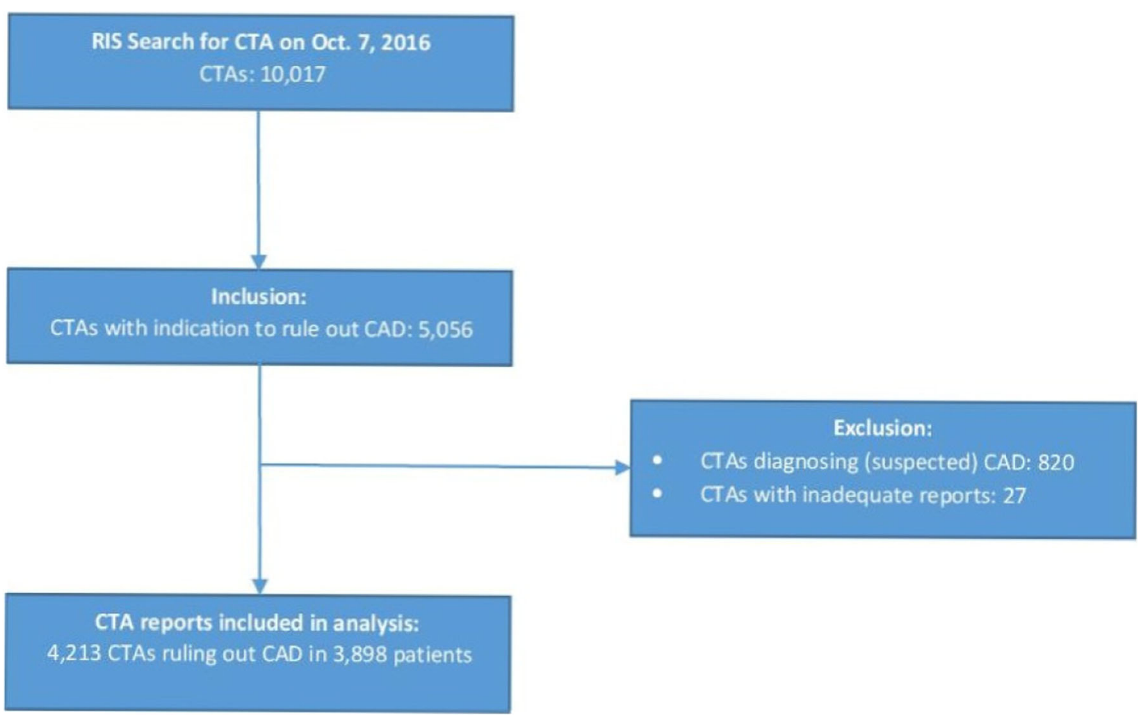


**Fig. 1** Flow chart of CTA report selection

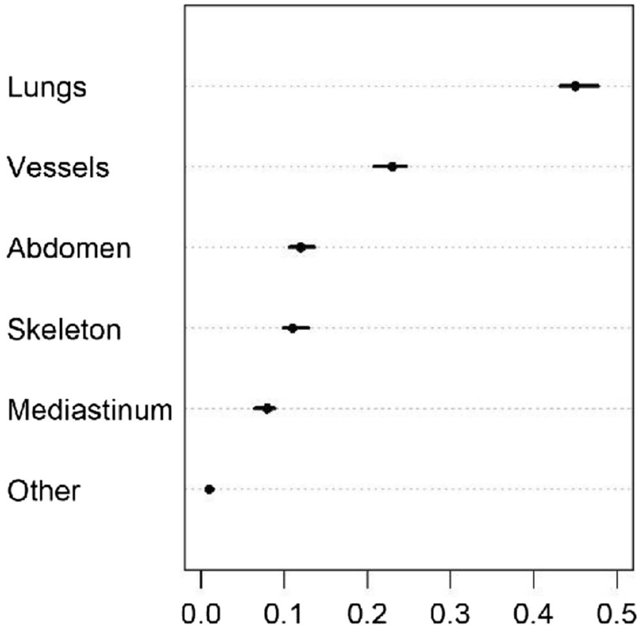


**Fig. 2** Relative distribution of extracardiac findings by body region

patient had breast cancer based on CT morphology (Table 2). Eleven of 14 malignancies were already known from the patients' histories when described in the CTA reports (ESM Table 2).

### ECFs in patients with chest pain

In the study cohort, 2330 of 3898 patients (59.7%) were symptomatic in terms of having chest pain. Of them, 7.9% (95% CI, 6.9–9.1%) had ECFs that might explain chest pain in those instances where CTA ruled out significant CAD, with spinal degeneration and hiatal hernia being the most commonly detected. All incidental malignant ECFs as well as 9 of 17 incidental urgent ECFs occurred in symptomatic patients including 5 patients with pulmonary infection, 1 patient with massive pleural effusion, and another patient with sarcoidosis. All ten patients with pulmonary embolism were symptomatic and considered in the analysis of incidental urgent ECFs. Two of them suffered from chest pain while the others had typical dyspnea as the leading symptom (Table 3). Hence, just those two patients were included when calculating the prevalence of ECFs potentially explaining chest pain.

### Temporal trends

The average number of ECFs per CTA was 0.4 (95% CI, 0.40−0.43) and increased from 0.1 (95% CI, 0.05–0.22) in 2003 to 0.8 (95% CI, 0.79–0.88) in 2014 (Table 4). The results of the Poisson regression presented in Table 5 indicate that the number of ECFs detected by CTA is statistically significantly influenced by patient age ($p < 0.001$) and cumulative professional experience in radiology of the CT readers with age being the covariate with the highest importance in terms of model fit. Sex ($p = 0.619$), the volume of contrast medium ($p = 0.092$), and the number of CT readers ($p = 0.128$) had no significant influence on the number of detected ECFs (Table 5).

## Discussion

The results presented here were obtained in a very large cohort of 3898 patients over a very long study period of 14 years. Thus, we could follow up initially suspicious ECFs for a mean of 5 years. To our knowledge, this study is the first to investigate whether CTA can contribute to the diagnosis in the large portion of patients with insignificant CAD but persistent symptoms.

CTA is suitable to rule out CAD; however, it is not uncommon to encounter ECF, which must be dealt with adequately. Reported prevalences range from 7% to 79% for overall ECFs and from 2% to 59% for clinically significant ECFs [10, 17–29]. Meta-analyses conducted by Karius, Flor, and Buckens et al calculated average (expected) prevalences of overall ECFs from 41.0% to 44.0%, while the mean prevalence of significant findings ranges from 13.0 to 16.0% [13, 30, 31]. Compared with these published data, the results for overall (30.2%) and relevant ECFs (2.8%) in our cohort without significant CAD are within the expected range but below average. We found previously unknown cancer in only 0.1% of our population, while the meta-analysis of Flor et al [30] reported incidental malignancies in 0.7% of patients. Each single study included, even those with significantly younger populations, revealed higher incidental malignancies compared with our results. Since lung cancer is most frequently detected in all studies, unfortunately not reported risk factors, such as smoking history, probably have a higher impact than age [13, 30]. Incidental malignant and urgent ECFs result in a change of diagnostic and therapeutic management based on CTA outcome. Lehmann et al reported that noncoronary incidental findings changed in-hospital management in 1.3% of patients with acute coronary syndrome [32]. Definite diagnostic workup of suspicious pulmonary nodules is important for detecting early lung cancer although screening trials have shown that 96.4% of those are false-positive findings [14]. Suspicious pulmonary nodules and consolidations are the main indication for further investigation resulting from CTA [11–14]. Thus, the Fleischner Society recently adjusted its management guidelines for incidentally detected pulmonary nodules to reduce unnecessary follow-up examinations and therefore costs and radiation exposure [33].

Moreover, our results show that CTA provides a large spectrum of differential diagnoses for noncardiac chest pain when significant CAD is ruled out (7.9%). Fass et al conclude that gastroesophageal reflux disease (GERD) is the most common contributing factor to noncardiac chest pain (NCCP) [34]. Although CT cannot diagnose GERD, demonstration of a hiatal hernia or esophageal wall thickening by CTA may point to an underlying reflux disease. Spalding et al [6] investigated 108

**Table 2** Relevant extracardiac findings

| Relevant ECFs | *N* | Prevalence | 95% CI |
|---|---|---|---|
| ECFs with recommendation for FU | | | |
| Pulmonary nodule/consolidation | 49 | 1.3% | 1.0–1.7% |
| Liver lesion | 15 | 0.4% | 0.2–0.6% |
| Chronic changes of lung parenchyma and bronchial system | 10 | 0.3% | 0.1–0.5% |
| Mediastinal lesion | 4 | 0.1% | 0.0–0.3% |
| Breast lesion/calcification | 3 | 0.1% | 0.0–0.2% |
| Aortic dilatation | 2 | 0.1% | 0.0–0.2% |
| Pleural lesion | 2 | 0.1% | 0.0–0.2% |
| Pulmonary infiltration/effusion | 2 | 0.1% | 0.0–0.2% |
| Hiatal hernia | 2 | 0.1% | 0.0–0.2% |
| Renal lesion | 2 | 0.1% | 0.0–0.2% |
| Enlarged/calcified lymph node | 2 | 0.1% | 0.0–0.2% |
| Dermal nodulus/lipoma | 1 | 0.0% | 0.0–0.1% |
| Esophageal thickening | 1 | 0.0% | 0.0–0.1% |
| Stenosis/occlusion of V. subclavia | 1 | 0.0% | 0.0–0.1% |
| No. of ECFs recommended for follow-up[a] | 96 | | |
| No. of patients with ECFs recommended for follow-up | 94 | | |
| No. of patients in study cohort | 3898 | | |
| Prevalence of ECFs recommended for follow-up[b] | | 2.4% | 2.0–2.9% |
| Malignant ECFs | | | |
| Lung cancer | 2 | 0.1% | 0.0–0.2% |
| Breast cancer | 1 | 0.0% | 0.0–0.1% |
| No. of incidental malignant ECFs | 3 | | |
| No. of patients with incidental malignant ECFs | 3 | | |
| No. of patients in study cohort | 3898 | | |
| Prevalence of incidental malignant ECFs[c] | | 0.1% | 0.0-0.2% |
| Urgent ECFs | | | |
| Pulmonary embolism | 10 | 0.3% | 0.1-0.5% |
| Pulmonary infection and inflammation | 5 | 0.1% | 0.1–0.3% |
| Massive pleural effusion | 1 | 0.0% | 0.0–0.1% |
| Sarcoidosis | 1 | 0.0% | 0.0–0.1% |
| No. of incidental urgent ECFs[d] | 17 | | |
| No. of patients with incidental urgent ECFs | 16 | | |
| No. of patients in study cohort | 3898 | | |
| Prevalence of incidental urgent ECFs[e] | | 0.4% | 0.3–0.7% |

[a] Two patients had two ECFs with recommendation for follow-up

[b] No. of patients with ECFs recommended for follow-up related to no. of patients in study cohort

[c] No. of patients with incidental malignant ECFs related to no. of patients in study cohort

[d] One patient had two incidental urgent ECF

[e] No. of patients with incidental urgent ECFs related to no. of patients in study cohort

patients with atypical chest pain with diagnostic workup not including CTA. Sixty-eight patients in this group (63%) were found to have noncoronary pathologies causing atypical chest pain. The causes identified included musculoskeletal (25), noncoronary cardiac (21), gastrointestinal (21), and respiratory (12) conditions. Fifty-one patients (47.2%) were referred for follow-up examinations, which is a substantially higher follow-up rate compared with the rate reported for patients examined by CTA [6]. GERD, esophageal dysmotility, and psychogenic disorders have been studied so far as relevant conditions causing NCCP [34–37]. Additionally, Spalding et al [6] as well as the results of our study identified musculoskeletal and

**Table 3** Extracardiac findings in symptomatic patients potentially causing chest pain

| ECFs potentially leading to chest pain | *N* | Prevalence | 95% CI |
|---|---|---|---|
| Muskulosceletal chest pain | | | |
| Extensive spinal degeneration | 102 | 4.4% | 3.6–5.3% |
| Bone metastasis/multiple myeloma | 3 | 0.1% | 0.0–0.4% |
| Mediastinal | | | |
| Hiatal hernia | 56 | 2.4% | 1.9–3.1% |
| Oesophageal wall thickening | 2 | 0.1% | 0.0–0.3% |
| Vascular | | | |
| Aortic aneurysm | 6 | 0.3% | 0.1–0.6% |
| Pulmonary embolism | 2 | 0.1% | 0.0–0.3% |
| Pulmonary or pleural chest pain | | | |
| Pleural effusion | 5 | 0.2% | 0.1–0.5% |
| Pulmonary infection | 4 | 0.2% | 0.1–0.4% |
| Lung cancer/metastasis | 3 | 0.1% | 0.0–0.4% |
| Other causes for chest pain | | | |
| Cholelithiasis | 2 | 0.1% | 0.0–0.3% |
| Breast cancer | 1 | 0.0% | 0.0–0.2% |
| No. of ECFs potentially causing chest pain[a] | 186 | | |
| No. of symptomatic patients with ECFs potentially causing chest pain | 185 | | |
| No. of patients with chest pain | 2330 | | |
| Prevalence of ECFs potentially causing chest pain[b] | | 7.9% | 6.9–9.1% |

[a] One symptomatic patient had two ECFs potentially causing chest pain

[b] No. of symptomatic patients with ECFs potentially causing chest pain related to no. of patients with chest pain

spine pathologies as the leading (potential) explanation for NCCP. Degenerative disc disease of the lower cervical and thoracic spine with accompanying radiculopathy may mimic anginal symptoms by causing anterior chest pain, even radiating to the upper extremities under certain circumstances [38]. Degenerative disc disease is frequently observed in age-equivalent cohorts. Notwithstanding, it is less common in the thoracic spine (males: 49.1%; females: 35.1%) than in cervical (males: 47.4%; females: 49.1%) or lumbar (males: 86.1%; females: 91.3%) regions and still remains asymptomatic in the majority of patients [39–41]. However, regarding the relatively high prevalence in symptomatic patients in our study, we suppose that degenerative spine changes are the nearest source of chest pain when a significant CAD is ruled out. Remarkably, all incidental malignant and the majority of incidental urgent ECFs occurred in symptomatic patients.

**Table 4** Temporal trend of average number of extracardiac findings per CTA and year

| Year of study period | No. of CTAs | Average No. of ECFs per CTA | 95% CI |
|---|---|---|---|
| 2000 | 1 | 1 | n. n. |
| 2001 | 1 | 0 | n. n. |
| 2002 | 7 | 0.1 | n. n. |
| 2003 | 48 | 0.1 | 0.00–0.21 |
| 2004 | 75 | 0.1 | 0.02–0.14 |
| 2005 | 195 | 0.1 | 0.08–0.19 |
| 2006 | 214 | 0.3 | 0.21–0.34 |
| 2007 | 158 | 0.4 | 0.30–0.54 |
| 2008 | 429 | 0.2 | 0.18–0.28 |
| 2009 | 562 | 0.3 | 0.23–0.33 |
| 2010 | 452 | 0.5 | 0.40–0.54 |
| 2011 | 528 | 0.3 | 0.25–0.37 |
| 2012 | 471 | 0.6 | 0.49–0.64 |
| 2013 | 418 | 0.8 | 0.67–0.85 |
| 2014 | 270 | 0.8 | 0.71–0.97 |
| **2000–2014** | **3829** | **0.4** | **0.40–0.44** |

Besides older patient age, the CT reader's professional experience is associated with the detection of more ECFs per CTA. The scientific focus on ECFs in the past years as well as the concomitant development of the Fleischner Criteria might have led to a higher awareness of extracardiac pathologies, probably contributing to a stepwise increase in the number of ECFs detected over the years.

## Limitations

We chose a retrospective study design to maximise the number of cases and the study period. Our RIS does not provide a

**Table 5** Results of Poisson regression

| Formula of Poisson regression: | N_ECF ~ sex + age + vol. of contrast medium + N reader + cumulative reader experience | | | | |
|---|---|---|---|---|---|
| Factors | Estimate | Std. deviation | Z-value | 95% CI | *p* value |
| (Intercept) | -3.795 | 0.198 | -19.134 | -4.185–3.407 | < 2e−16 |
| Factor(sex)f | 0.026 | 0.052 | 0.497 | 0.076–0128 | 0.619 |
| Factor(age) | 0.036 | 0.002 | 15.596 | 0.031–0.040 | < 2e−16 |
| Factor(vol_contrast medium) | -0.002 | 0.001 | -1.686 | -0.004–0.000 | 0.092 |
| Factor(n_reader) | 0.104 | 0.068 | 1.522 | -0.032–0.235 | 0.128 |
| Factor(cum_reader_exp) | 0.005 | 0.001 | 8.674 | 0.004–0.006 | < 2e−16 |

databank with the option to export detailed information of the CTA protocol performed, including information on small vs. large FOV application. Hence, the assessment of ECFs is supposed to be inconsistent over the large study period. Moreover, ECFs were captured from the reports at the initial time of the scan without rereading CTA. Consequently, the statement of non-relevant ECFs in particular is strongly dependent on what the investigator found worth reporting. The spectrum and frequency of ECFs identified as potential causes of chest pain are based on theoretical considerations rather than clinical data not having sufficient information on the quality, quantity, and location of chest pain. This is why we refrained from re-correlating CTA images again, especially regarding chest pain and the frequently observed degenerative spine. This might have led to overestimation of ECFs potentially causing chest pain. The fact that chest pain in patients with insignificant CAD can also be caused by noncoronary cardiac pathologies was not considered in our analysis. Both in- and outpatients were included. Follow-up examinations in the latter group were consistently performed on an outpatient basis, resulting in a lack of data in our electronic patient files. Consequently, 65 of 95 (68.4%) recommended follow-up examinations were not available despite an adequate observational period. This lack of data probably led to additional underreporting of early malignancies. A total of 10.0% of all CTAs could not be used for multivariate analysis of temporal trends because information on at least one covariate was not available. The study population is subject to selection bias because of nonrandomised recruitment. Besides patient age and professional experience of CT readers, the occurrence of ECFs is certainly influenced by other factors such as comorbidity, individual risk factors (e.g., smoking), and use of large FOV reconstruction. Unfortunately, these factors could not be considered here because of insufficient data.

## Conclusion

Our results show that reading CTA for extracardiac pathologies reveals incidental urgent and malignant pathologies as well as a broad spectrum of differential diagnoses for chest pain in symptomatic patients even in a much larger number. On the one hand, this may prevent patients from a missed diagnosis or delayed therapy and allows the initiation of efficient diagnostic testing and therapy on the other hand. Thus, reading CTA for ECF pathologies is recommended especially in patients with chest pain from our point of view. However, further prospective investigation should be done to clarify the role of frequently observed degenerative spine changes in mimicking chest pain when a significant CAD is ruled out.

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## Compliance with ethical standards

**Guarantor** The scientific guarantor of this publication is Prof. Dr. Marc Dewey

**Conflict of interest** The authors of this manuscript declare relationships with the following companies:

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Prof. Dewey is a consultant to Guerbet and one of the principal investigators of multicentre studies (CORE-64 and 320) on coronary CT angiography sponsored by Toshiba Medical Systems. He is also the editor of Coronary CT Angiography and Cardiac CT, both published by Springer, and offers hands-on workshops on cardiovascular imaging (www.ct-kurs.de). Prof. Dewey is a consultant to the editor of Radiology and an associate editor of European Radiology. Institutional master research agreements exist with Siemens Medical Solutions, Philips Medical Systems, and Toshiba Medical Systems. The terms of these arrangements are managed by the legal department of Charité-Universitätsmedizin Berlin.

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**Methodology**
• retrospective

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