Journal Pre-proofs

Research article

Coronary Computed Tomography Angiography in acute chest pain: a sustainable model with remote support

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PII: S0720-048X(22)00127-9
DOI: https://doi.org/10.1016/j.ejrad.2022.110277
Reference: EURR 110277

To appear in: *European Journal of Radiology*

Received Date: 21 August 2021
Revised Date: 20 February 2022
Accepted Date: 20 March 2022

Please cite this article as: N. Galea, R. Bellu, F. Catapano, L. Marchitelli, G. Cannavale, P. Sedati, C. Colmo, A. Zamana, M. Arboit, X. Raspanti, A. Roncacci, C. Catalano, M. Francone, Coronary Computed Tomography Angiography in acute chest pain: a sustainable model with remote support, *European Journal of Radiology* (2022), doi: https://doi.org/10.1016/j.ejrad.2022.110277

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Supportive foundations: No financial support was provided for this study.

Conflict-of-interest statement: No conflicting interest to declare.

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Highlights

- CCTA examination in the ED allows to rule-out ACS in patients with acute chest pain
- Causes of acute chest pain other than CAD can be revealed by CCTA
- CCTA enables to reduce both patient's discharge time and risk of misdiagnosis
- Risk stratification of MACE can be improved using CCTA evaluation
- A partial teleradiology based 24/7 CCTA model is sustainable even in small centers

Abstract:

Purpose: To propose a sustainable model of coronary computed tomography angiography(CCTA) use in acute coronary syndrome(ACS) in emergency department(ED) using a partially based teleradiology reporting model. We also analyzed impact of the protocol on short- and long-term patient's outcome.

Methods: During a 12-month period, 104 consecutive patients admitted to the ED for acute chest pain(ACP) with low-to-intermediate risk of ACS were selected and underwent CCTA. Medical reporting was based on a model combining on-site physician and a remote radiologist supported by a web client-based teleradiology system, covering a 24/7 service. CCTA findings were correlated with the incidence of major adverse cardiovascular events(MACEs) over a 5-year follow-up.

Results: CCTA ruled-out CAD in 76 patients(73.1%). Moderate(7.7%) to severe(19.2%) CAD was identified in 28 patients who were directly referred to functional tests or invasive angiography. The mean discharge time was 10.8±5.8 hours; patients with absent to mild disease were safely and quickly discharged. Remote reporting using a teleradiology platform was performed in 82/104 cases(78.9%), with slight impact on patient's discharge time(10.4 ± 5.6 vs. 12.1 ± 6.1 hrs, p: 0.24). MACEs at 6-month and at 5-year follow-up were 0.96% (n = 1/104) and 15.5% (n=14/90).

Conclusion: CCTA assessment of patients with ACP enables to quickly rule-out ACS, avoiding waste of time and resources, to identify patients with obstructive CAD which should be referred to subsequent tests and to stratify the risk of MACEs at short and long time. A partial teleradiology based 24/7 CCTA service is feasible and sustainable, even in small ED.

Keywords: Coronary Computed Tomography Angiography; Acute Chest Pain; Acute Coronary Syndrome; Coronary Artery Disease; Emergency Department; Teleradiology.

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Abbreviations

ACP: Acute Chest Pain

ACS: Acute Coronary Syndrome

CABG: Coronary Artery Bypass Grafting

CACS: Coronary Artery Calcium Score

CAD: Coronary Artery Disease

CAD-RADS: CAD Reporting and Data System

CCTA: Coronary Computed Tomography Angiography

CMR: Cardiovascular Magnetic Resonance

CPR: Curved Planar Reformat

CPU: Chest Pain Unit

CT: Computed Tomography

CX: Circumflex artery

ECG: Electrocardiogram

ED: Emergency Department

ESC: European Society of Cardiology

FFRCT: Fractional Flow Reserve - derived CCTA

HR: Heart Rate

hs-cTn: high-sensitive cardiac Troponin

ICA: invasive coronary angiography

LAD: Left Anterior Descending artery

LM: Left Main

MACESS: Major Adverse Cardiovascular Events

MPR: Multiplanar Reconstructions

NICE: National Institute for Health and Care Excellence

NSTEMI: non-ST Elevation Myocardial Infarction

PCI: Percutaneous Coronary Intervention

RCA: Right Coronary Artery

SCOT-HEART: Scottish Computed Tomography of the HEART trial

Introduction

Acute chest pain (ACP) syndrome includes a large and heterogeneous spectrum of pathological conditions ranging from mild benign affections to life-threatening cardiothoracic emergencies including acute coronary syndrome (ACS), aortic dissection, massive pulmonary embolism and tension pneumothorax [1]. Unstable angina and non-ST elevation myocardial infarction (NSTEMI) are closely related conditions with similar pathogenesis, which can present without significant ECG abnormalities or laboratory data suggestive of ischemic myocardial injury, and the diagnosis often requires the integration of serial evaluation of the ECG, troponin levels, and several provocative testing results, long observational time in the emergency department (ED) [2] and increase of healthcare costs [3]. Nevertheless, there is a still significant rate of 4-8% of subjects with myocardial infarction inappropriately discharged from the ED [4].

Several clinical trials [5-7] have proved that use of CCTA allows a higher rate of patient's discharge from ED with shorter length of stay and consequent cost saving compared to the standard of care approaches [8], and the last update of European Society of Cardiology (ESC) guidelines for the management of ACS, considers CCTA the best option in symptomatic patients with low-to-intermediate clinical likelihood of unstable angina, thanks to its high negative predictive value to exclude obstructive CAD [9].

However, unanimous consensus on the large-scale use of this protocol has not been reached yet, considering several disadvantages and limitations of its applicability in clinical practice [10], like the need for trained cardiac radiologists who provide 24/7 service in the ED. A possible solution to this problem could be the wide and effective diffusion of client platforms, which may enable the remote real-time consultation of CCTA images by dedicated cardiac radiologists in support to local general radiologists [11,12].

Our purpose was to evaluate the clinical impact and organizational sustainability of a Chest Pain Unit (CPU) model based on the use of CCTA to rule out obstructive CAD, that relies on the availability of a team of cardiac radiologists providing 24/7 onsite or remote consultation.

As an additional clinical endpoint, we also recorded short- and long-term major cardiovascular events (MACE), occurred within 5 years of CCTA examination.

Materials and methods

Study Population

Patients were consecutively selected from a cohort of 637 subjects (> 18 years) with ACP admitted at the ED of Abano Terme Hospital (Italy), an emergency and trauma urban center, during a 12-month period (April 2015 - March 2016). Patients diagnosed with ST-elevation myocardial infarction (STEMI) were identified and treated according to the current guidelines of the American Heart Association [13]. The remaining patients presenting "ACP of possible cardiac origin" were addressed to CPU and examined by on-call cardiologists, which assessed preliminary risk stratification according to the HEART Clinical Score system, a clinical tool for risk stratification of patients with ACP validated in a multicenter prospective study, composed of five parameters, including history, ECG, age, risk factors and troponin [14].

Schematic representation of eligibility criteria applied for CCTA examination is displayed in Figure 1.

Briefly, we stratified patients in low (HEART score 0-3) and high risk (HEART score 4-10), and then selected patients to undergo CCTA after a 0/3 hour observation, as follows:

- low risk individuals with hs-cTn within normal range at admission and increasing;
- low risk individuals with hs-cTn rising upper than 99th percentile of normal range at admission and not doubling;
- high risk individuals with negative hs-cTn at first dosage remaining in normal range at second sample.

Exclusion criteria included estimated glomerular filtration rate (eGFR) less than 30 ml/min/1.73 m2 or history of allergy to iodinated contrast agent, known CAD or previous coronary revascularization, irregular heart rhythms such as atrial fibrillation and/or heart rate (HR) persistently higher than 70 bpm despite pharmacological strategies, pregnancy or breastfeeding. After CCTA, were excluded from the study patients with extensive coronary artery calcifications and examinations with poor image quality (e.g. motion artefacts).

The institutional ethical committee approved the study protocol and all patients provided written informed consent.

Patient's preparation

Patients with HR > 70 bpm received 50 mg or 100 mg oral metoprolol, according to their BMI, at least one hour prior to CCTA with a HR target of less than 65 bpm or, alternatively, an intravenous bolus of esmolol 1 or 2 mg/kg was administered just after scout acquisition. HR control in patients with general contraindications to beta-blockers was obtained using oral ivabradine (15 mg orally two hours before CCTA scan).
Immediately prior to CCTA scanning, sublingual nitroglycerin (preferably 2 capsules, equal to 0.8 mg or 1.0 mg as available, or spray [2 puffs, equal to 0.8 mg]) was also routinely administrated if systolic blood pressure was ≥100 mmHg and no further contraindications were present.

CCTA scanning technique

All patients were scanned with a last generation multi-detector CT scanner (Aquilion One Vision Edition, Canon Medical Systems Corporation, Tokyo, Japan) equipped with a gantry rotation of 0.275 seconds and 320 detector rows (640 unique slices), covering 16 cm in a single rotation (slice thickness: 0.5 mm; half scan reconstruction). The scanner was equipped with the third-generation iterative dose reconstruction software AIDR 3D; tube voltage was fixed at 120 or 100 kVp with automated tube current mA modulation. Prospective gating was performed in all patients with a HR lower than 70 beats per minute (bpm); in case of an arrhythmia, CT scanner automatically adjusted the scan and acquired the next normal heartbeat with ^{SURE}Cardio Prospective application. The CT acquisition technique used a volume scan mode non-spiral acquisition with no table motion during scanning. Contrast injection protocol consisted of the administration of a bolus of 55 ml of high concentration contrast agent (Iomeprol 400 mg iodine/ml; Iomeron 400, Bracco, Milan, Italy) followed by 50 ml of saline flush, both injected at 5.5 ml/sec of flow rate.

Images analysis and reporting optimization

A 24hours/7days coverage for CCTA exam acquisition and reporting was warranted by the continuous availability "on-site" or "on-call" of a cardiac radiologist, ensured by the rotation of 10-years experienced readers covering 36-hours "on-site" within the hospital (in addition to the routine daily activities) and the remaining 5.5 days on-call by remote (exclusively available for CCTA examinations) per week, with a monthly on-site commitment of 13-14 shifts of 12 hours per month. All general radiologists and technicians received a specific training to guarantee optimal CCTA image acquisition.
When the CCTA was carried out by a remote cardiac radiologist in cooperation with an on-site general radiologist, the latter was in charge of obtaining informed consent, premedicating the patient (e.g. beta-blockers or nitrates), planning the CT protocol and assisting during contrast media administration.
The tele-radiology reporting relied on high-performing laptop computer equipped with retina display (resolution 2060x1600 pixels, at 227 pixels per inch) and high-speed internet connection, and a dedicated web-based client software with CCTA package (Vitrea Core Version 6.7; Vital Images Inc, USA) for image viewing, analysis and reporting. Coronary arteries stenoses were classified on basis of percentage of vessel diameters reduction as minimal (<25%), mild (25-49%), moderate (50-69%), severe (70-99%) or occlusive (100%). All CCTA exams have been categorized into six categories according to CAD Reporting and Data System (CAD-RADS) classification [15], considering the highest grade of coronary stenosis detected in any vessel. A visual assessment of coronary plaques was also carried-out in all cases, categorizing lesions based on density composition as soft, mixed and calcified.
The whole CCTA-related process, from the acquisition phase to post-processing and production of final radiological report was optimized to speed-up the diagnostic workup and provide the fastest communication to the referring physician of the CPU.

Impact of CCTA findings on clinical management

In patients with none, minimal or mild coronary stenoses ACS was excluded and other potential causes of ACP have been investigated before discharge. In patients with severe or occlusive stenoses as well as left main lesions with a diameter reduction $\geqslant$ 50% invasive coronary angiography (ICA) has been recommended.

Patients with moderate coronary lesions underwent a further 24-48 hours observation with serial hs-cTn dosage, and then were referred for a functional test (exercise treadmill test or stress SPECT imaging) or ICA based on the clinical and serological evolution.

The decision to perform coronary revascularization was established according to the current appropriateness criteria [16].

Clinical follow-up

A standardized follow-up telephone interview was performed 30-days, 6-month and 5-years after the discharge from ED, verifying the occurrence of MACEs, defined as the composite of cardiac death, non-fatal myocardial infarction, coronary revascularization by Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG) at least 6 weeks after CCTA, stroke, and hospitalization because of heart failure. If a patient experienced >1 MACEs, the first event was chosen. Furthermore, all eventual new re-hospitalization has been carefully evaluated to verify all events potentially attributable to cardiac origin, such as recurrence of ACP resulting in medical consultation or diagnostic testing.

Statistical analysis

Data were analyzed with SPSS software version 20.0 (SPSS Inc., Chicago, Illinois, USA). All the data are presented as counts and percentages for categorical data and means ± standard deviation for continuous data and continuous data distributions were tested for normality using Shapiro-Wilk normality test. The comparison between times was performed using Student's t test. The statistical significance was set at two-sided $p < 0.05$.

Survival curves were constructed using the Kaplan–Meier method and between groups comparison was made using the log-rank test. A p-value < 0.05 was considered statistically significant.

Results

Clinical data

From an initial study population of 637 individuals admitted with ACP to the ED, a selected cohort of 107 patients was eligible and performed CCTA. Among these patients, 3/107 patients were excluded due to poor image quality (n: 2), inadequate for coronary assessment, or heavy calcifications (n: 1) in the coronary tree. The final cohort consisted of 104 individuals. Patient's mean age was 63.2 ± 11.2 years (range: 37 - 86 years) with a prevalence of male subjects (68 males and 36 females). All patients underwent CCTA within 6.2 ± 3.1 hours from admission. Remote reporting using a teleradiology platform was performed in 82/104 cases (78.9%), 49 of which were performed overnight, with a slight, but non-significant, impact on patient discharge time (10.4 ± 5.6 vs. 12.1 ± 6.1 hrs, p: 0.24). The mean discharge time in patients who performed CCTA was 10.8 ± 5.8 hours.

Detailed CCTA patient's demographics and risk factors are reported in Table 1.

Overall, 100% of patients had a complete follow-up performed by telephone call at six months from the discharge, and MACE rate was 0.96% (n = 1/104).

At the long-term evaluation, with mean follow-up duration of 5.63 ± 0.60 years, 10 patients were excluded because they could not be reached by telephone and 4 because they died of noncardiac causes.
Among 90/104 patients MACEs occurred in 14 patients (15.5%).

CCTA findings and follow-up evaluation

CCTA ruled-out obstructive CAD in 76 patients (73.1%), showing absent to minimal disease in 58 patients and mild stenoses in 18 patients. The remaining 28 patients with moderate-to-severe lesions (26.9%) showed a predominance of a significant single-vessel disease (71%, n=20/28), 21% two-vessel disease (n= 6/28) and only two patients had three vessels obstructive CAD (7%). Detailed CCTA findings are illustrated in Table 2.

All patients with non-obstructive CAD were discharged from the ED in the shortest time possible after a final clinical evaluation at CPU. Among these, 6 patients were hospitalized after CPU evaluation because of persistent symptoms (two with a final diagnosis of acute myocarditis (Figure 2), one with Takotsubo syndrome, and one with peptic ulcer), or because CCTA identified other potential causes of chest pain (one patient with pulmonary embolism and another with pneumonia). In this subgroup, only one subject had a new short-term admission to ED due to dyspnea and palpitations with no troponin raise or ECG abnormalities and final diagnosis of anxiety disorder. Absence of obstructive CAD at CCTA translates into a high negative predictive value of 100% to exclude 30 days MACEs in ACP patients. Data collected during the long-term follow-up period reported only 1/76 MACE in this group at 6 months (1.3%), one patient re-admitted to ED with diagnosis of NSTEMI, and 8/67 MACEs at 5 years (11.9%): three myocardial infarctions successfully revascularized, two hospitalizations due to pulmonary edema in congestive heart failure, one stroke and two acute heart failures.

All patients with significant coronary stenoses at CCTA and 3 out of 8 patients with moderate stenosis underwent ICA (Figure 3 and 4). Among these, 19/23 underwent PCI, after invasive hemodynamic characterization of all lesions. Four patients underwent coronary bypass graft surgery, two with a significant two-vessel disease involving proximal LAD, one with a left main coronary artery severe stenosis and one with a three-vessel disease with culprit lesion involving CX. No major peri-procedural complications occurred in patients which underwent ICA neither in patients addressed to cardiac surgery. In this group no MACE was reported at 6-month follow up (0/23), whereas 5/18 (27.7%) experienced MACEs at 5 years (Figure 5).

The other 5 patients with moderate CAD at CCTA underwent additional immediate monitoring at CPU with serial myocardial necrosis enzyme assays and ECG and then discharged with indication to perform an elective stress test within 1 week. None of the patients which performed stress tests reported inducible myocardial ischemia, and both 30-day and 6-month follow-up revealed no MACE or new admissions to the ED in this group. At 5-year evaluation 1 patient had STEMI treated with PCI.

Discussion

Our pilot study demonstrates the feasibility and usefulness of partial teleradiology based 24/7 CCTA service to rule out ACS in patients presenting ACP and the benefits in terms of risk stratification for MACEs.

Although various large clinical trials have demonstrated the role of CCTA in selecting patients that can be safely discharged from the ED [5, 17, 18], in diagnosing obstructive CAD or in predicting MACEs, the employment of teleradiology system in this setting has not been documented yet.

This is a single-center prospective cohort study conducted in a first-level, small urban ED with an approximate annual volume of 35.000 visits/year. The center is equipped with an active 24/7 surgical and clinical guard but is not provided with hemodynamic unit, therefore, patients who require ICA are transferred into the local reference hospital in Padua. In this ED, the radiology coverage is warranted by the rotation of one dedicated radiologist with generalist expertise per 12-hour shift. The proposed model was conceived considering the number of daily CCTA exams requested, that does not justify the costs of extra on-site personnel in addition to the general radiologist, the limited availability of CCTA experts in the local radiology market and the need to guarantee appropriate time of execution and reporting of urgent CCTA exams.

Our organizational model was set-up to respond to the clinical requests of a small urban center with specific specialization in cardiac imaging and no cath lab availability.

This reflects the fact that our weekly coverage consisted on the onsite availability of a dedicated radiologist 36h per week plus a remote assistance and reporting for the remaining 5.5 days, covered by a the rotation of three cardiac radiologists on-call.

The use of teleradiology in ED is a hotly debated issue with great prospects but still uncertain and unclear implications. Image teleconsultation and remote reporting systems have been massively implemented over the last decade [19], also driven by a market that increasingly pushes the storage and sharing of data on cloud.

Studies comparing radiologic images reading on laptop and tablet with standard workstations did not show significant differences in diagnostic accuracy [20]. However, there are still concerns about the quality assurance of off-site exams, which requires high preparation and reliability of the technician [21, 22].

In our model a trained technician performs the exams under the supervision of the on-site radiologist, and teleradiology serves as a support system.

In this perspective, a great effort was made to ensure the appropriate training of the entire staff to guarantee optimal image quality, also in unfavorable conditions. This goal was simplified by the use of a latest generation scanner, based on a wide coverage scanning technique, which allows the acquisition of the entire cardiac volume in a single heartbeat, with limited motion artefacts and no step artefacts, a particular issue in not well-prepared or uncooperative patients, as frequently found among individuals with ACP. This was also confirmed by the very low number of non-diagnostic exams in our cohort.

Interestingly, in our study remote-reporting times proved to be faster than on-site reporting times even though no significantly (2.4 ± 4.8 hrs vs 3.6 ± 5.3 hrs, p: 0.33), probably because of the volume of examinations that the on-site radiologist has to manage, with variable priority and complexity according to the routine ED activity.

These faster discharge times represent an encouraging signal towards the effectiveness of the proposed model, that should be confirmed in larger cohorts.

On this basis, in our model, cardiac radiologists were available exclusively for CCTA examination, thus avoiding the potential overload of examinations deriving from general "on-call" activities.Another limitation to the sustainability of CCTA in the ED is the potential increase in requests for further examinations induced by CCTA findings. Since the 2016 National Institute for Health and Care Excellence (NICE) update of the stable chest pain guideline, there has been growing debate about the management of patients with intermediate lesions at CCTA [23]. Several studies so far have showed an increase in down-stream testing, including additional functional testing and specifically ICA in the CCTA

groups [10]. As previously assumed [24, 25], the solution could be an appropriate and rigorous patient selection. On this aim, latest technologies, such as CT perfusion and FFR-derived CCTA (FFRCT), could further improve patient selection to be referred to ICA, allowing a one-stop shop anatomical and functional assessment.
In our flowchart, we stratified patients in low and high risk according to the HEART score system, and then selected patients to undergo CCTA after a 0/3 hour observation, as described above.
In the last update of *ESC guidelines for the management of ACS in patients presenting without ST-segment elevation*, a new rapid rule-in and rule-out algorithm, the so-called 0/1h, in the evaluation of ACP patients in the ED has been proposed, which recommends the use of CCTA in specific settings [9].

Although the 0/1h ESC algorithm proved to be associated with significantly shorter length of stay in the ED and high discharge rates without excessive use of diagnostic resources [26], in a recent prospective study, the HEART score proved to be better at detecting patients with a low risk of MACEs at 30 days than the ESC 0/1h algorithm [27].
In our study, patients with CCTA coronary stenosis lower than 50% were considered not likely affected by an ACS and therefore quickly and safely discharged from the ED after a final evaluation at CPU, with no indication to further testing. As a demonstration of the effectiveness of our model, no MACE or death during the 30-days follow-up period was reported, suggesting that the earlier discharge in this group did not result in missed diagnosis; at 30-days follow-up only one new access in the ED was recorded in this group due to dyspnea and palpitations with final diagnosis of anxiety disorder. Our results are in line with previous studies that have demonstrated an extremely low 30-day MACE rate in this group of patients, suggesting that further testing should not be indicated [28, 29].
Moreover, in this group, CCTA proved to be crucial in identifying other underlying causes of ACP, and/or allowed correct referral to the next imaging by limiting the flow of downstream examinations, as in the case of Takotsubo and myocarditis, both diagnosed with subsequent cardiac magnetic resonance (CMR).
All patients with severe CAD at CCTA and 3 out of 8 patients with moderate stenosis underwent ICA with agreement between stenosis degree and angiographic findings and consequent treatment of the culprit lesions. These patients with obstructive CAD but no indication for urgent ICA would certainly have had a more complex diagnostic workup in the ED, with several functional tests and/or long observation times. It is also reasonable to assume that some of them could have been mistakenly discharged and presented MACEs in the following days.
The remaining 5 patients with moderate CAD at CCTA in our population were discharged with indication to perform an elective stress test within 1 week. None of the subsequent stress tests performed reported signs of functional myocardial ischemia, and the 6-month follow-up period revealed no MACE or new ED admissions, supporting the safety of the CCTA-based strategy in this group.
Furthermore, for a more complete assessment of prognostic value, we performed two long-term follow-ups at 6 months and 5 years, reporting MACE rates of 0.96% (n=1/104) and 12.6% (n=14/90), respectively.
Our findings are in line with results of the Scottish Computed Tomography of the HEART trial (SCOT-HEART), which showed a reduction in fatal and non-fatal myocardial infarction in the CCTA group compared to the group randomized to standard care at both 2- and 5-years follow-up, without an increase in ICA and/or revascularization [30].
Recently, Won Lee et. al [31] have demonstrated the incremental prognostic value of CAD-RADS category compared with clinical risk factors and calcium scoring (CACS) to predict MACEs in patients with ACP, further reinforcing our decision not to perform CACS for dosimetric considerations in the absence of increased diagnostic benefit [32].
They also have shown that higher CAD-RADS categories are independent predictors of MACE. Proportionally, we reported similar rates of MACEs in the non-obstructive CAD group (CAD-RADS 0-2) during the short-term follow-up

(1% at 3-month Vs 1.3% at 6-month) but a higher rate of MACEs in the long-term evaluation, probably due to both the smaller population size and the longer follow-up time in our study (median 31.5 months vs 67 months).

We recognize that many limitations affect our study. First, this is a pilot study with small study population and no control group managed according to the standard-of-care protocol, therefore the incontrovertible benefit of our model is not proved but only presumable. We did not report modifier V (presence of "vulnerable" plaque features) for CAD-RADS, although the presence of high-risk plaque signs was still considered in clinical management, and we did not analyze the impact of plaque composition on patient management and prognosis.

Finally, there is lack of a cost-effectiveness analysis, which it should also consider additional downstream tests demanded using the CCTA, with possible increase in costs and discomfort for the patients.

Conclusion

CCTA improves the evaluation of ACP in ED by assessing the presence of coronary stenosis requiring further investigation or invasive procedure, improving risk stratification of MACE and helping in detecting extra-coronary causes. Furthermore, CCTA allows to speed-up patient's discharge and minimize risks of incorrect diagnoses, with eventual related health-care costs reduction and improved individual therapeutic management.

A partial teleradiology based 24/7 CCTA service is feasible and sustainable, even in small ED with low number of accesses.

Figure and Table Legend

Table 1 Demographic and clinical characteristics of CCTA patients

Demographic and clinical characteristics	
Age: years - mean ± SD	63.2 ± 11.2
Sex: Female - n (%)	36 (34.6)
Cardiovascular risk factors - *n (%)*	
Hypertension	54 (52)
Diabetes mellitus	10 (10)
Dyslipidemia	50 (48)
Former or current smoker	47 (45)
Family history of premature coronary artery disease	33 (32)
Number of cardiovascular risk factors – *n (%)*	
0 or 1	42 (40)
2 or 3	58 (56)
≥4	4 (4)
HEART Score – *n (%)*	
0 - 3	*71 (68)*
≥4	*33 (32)*
Relevant prior medication – *n* (%)	
Aspirin	26 (25)
Beta-blocker	17 (16)
Statin	31 (30)
Initial presentation in emergency department	
Main symptom – *n* (%)	
Chest pain or anginal equivalent	94 (90)
Arm, jaw, shoulder, or epigastric pain	4 (4)
Shortness of breath	3 (3)
Other	3 (3)
Heart rate – beats per minute, mean ± SD	68.4 ± 12.6
Blood pressure – mmHg, mean ± SD	
Systolic	136.2 ± 24.9
Diastolic	85.4 ± 15.2
Body mass index - mean ± SD	28.5 ± 4.3
ECG Changes - n (%)	
No changes	79 (76)

SD: Standard Deviation; hs-cTn: high sensitive cardiac Troponin

Table 2 CCTA features and hospitalization timeline

CCTA Features	
Per patient	
No stenosis, n (%)	38 (36.5)
Minimal (<25%), n (%)	20 (19.2)
Mild (25-49%), n (%)	18 (17.3)
Moderate (50-69%), n (%)	8 (7.7)
Severe (70-99%), n (%)	20 (19.2)
Occlusion (>99%), n (%)	0 (0)
Per vessel	
LM	
No stenosis, n (%)	84 (80.8)
Minimal (<25%), n (%)	10 (9.6)
Mild (25-49%), n (%)	8 (7.7)
Moderate (50-69%), n (%)	0 (0)
Severe (70-99%), n (%)	2 (1.9)
Occlusion (>99%), n (%)	0 (0)
LAD	
No stenosis, n (%)	40 (38.5)
Minimal (<25%), n (%)	22 (21.2)
Mild (25-49%), n (%)	14 (13.5)
Moderate (50-69%), n (%)	12 (11.5)
Severe (70-99%), n (%)	16 (15.4)
Occlusion (>99%), n (%)	0 (0)
CX	
No stenosis, n (%)	72 (69.2)
Minimal (<25%), n (%)	12 (11.5)
Mild (25-49%), n (%)	16 (15.4)
Moderate (50-69%), n (%)	4 (3.9)
Severe (70-99%), n (%)	0 (0)
Occlusion (>99%), n (%)	0 (0)
RCA	
No stenosis, n (%)	76 (73.1)
Minimal (<25%), n (%)	4 (3.9)

CCTA: Cardiac Computed Tomography Angiography; LM: Left Main; LAD: Left Anterior Descending Artery; Cx; Circumflex Artery; RCA: Right Coronary Artery; CAD-RADS: Coronary Artery Disease Reporting and Data System; SD: Standard Deviation

Fig. 1 CCTA-based Diagnostic Pathway

ACP: Acute Chest Pain; hs-cTn: high sensitive cardiac Troponin; CCTA: Cardiac Computed Tomography Angiography; ACS: Acute Coronary Syndrome; PCI: Percutaneous Coronary Intervention

Fig. 2

47-year-old female admitted to ED with ACP, increased troponin level with a 9-12h peak. CCTA showed absence of coronary plaques (A, B). To further evaluate the cause of ACP and increased troponin levels, the patient underwent a CMR within one week from the acute event, which showed transmural area of edema at STIR images (C) in the infero-lateral segment with corresponding LGE area (D). Myocarditis diagnosis was established.

CCTA: Cardiac Computed Tomography Angiography; ED: Emergency Department; ACP: Acute Chest Pain; ECG: Electrocardiogram; CPR: Curved Planar Reformation; CMR: Cardiac Magnetic Resonance; STIR: Short-Tau Inversion Recovery; LGE: Late Gadolinium Enhancement

Fig. 3

56-year old male patient admitted to ED for ACP. Physical examination and basal ECG were normal (a). Laboratory test found troponin T equal to 13 ng/L not doubling at 3-hour (b). 3D volume rendering (c-d) and CPR (e-f) show soft-density atherosclerotic plaque causing a severe stenosis in distal LAD (white arrows). The patient was addressed to ICA(g), which confirms the subocclusion (black arrow), and treated with angioplasty and stenting.

ED: Emergency Department; ACP: Acute Chest Pain; ECG: Electrocardiogram; CPR: Curved Planar Reformation; LAD: left Anterior Descending Coronary Artery; ICA: Invasive Coronary Angiography

Fig. 4

74-year-old female admitted to ED with tachycardia, constrictive precordial pain and right arm paresthesia; paroxysmal supraventricular tachycardia during hospitalization. Laboratory test found troponin T equal to 16.6 ng/L not doubling at 3-hour (c). 3D volume rendering (a) and CPR (b) show coronary artery atherosclerotic plaque causing severe stenosis in first diagonal artery (b- left side white arrow) and obtuse marginal artery (b- right side white arrow). The patient was addressed to ICA (f), which confirms the CCTA findings (black arrows), with subsequent stenting of both vessels.

ED: Emergency Department; CPR: Curved Planar Reformation; CCTA: Cardiac Computed Tomography Angiography; ICA: Invasive Coronary Angiography

Fig. 5 Patient outcomes at 30-days, 6-months and 5-years follow-up

(a) Flowchart showing patient outcomes stratified by CCTA results. (b) Kaplan-Meier curves of MACE-free survival in patients with (yellow line) and without (red line) significant stenosis (log rank <0.05).

PT: Patients; ED: Emergency Department; ACP: Acute Chest Pain; CCTA: Coronary Computed Tomography Angiography; CAD: Coronary Artery Disease; MACE: Major Adverse Cardiac Events; CPU: Chest Pain Unit; ICA: Invasive Coronary Angiography

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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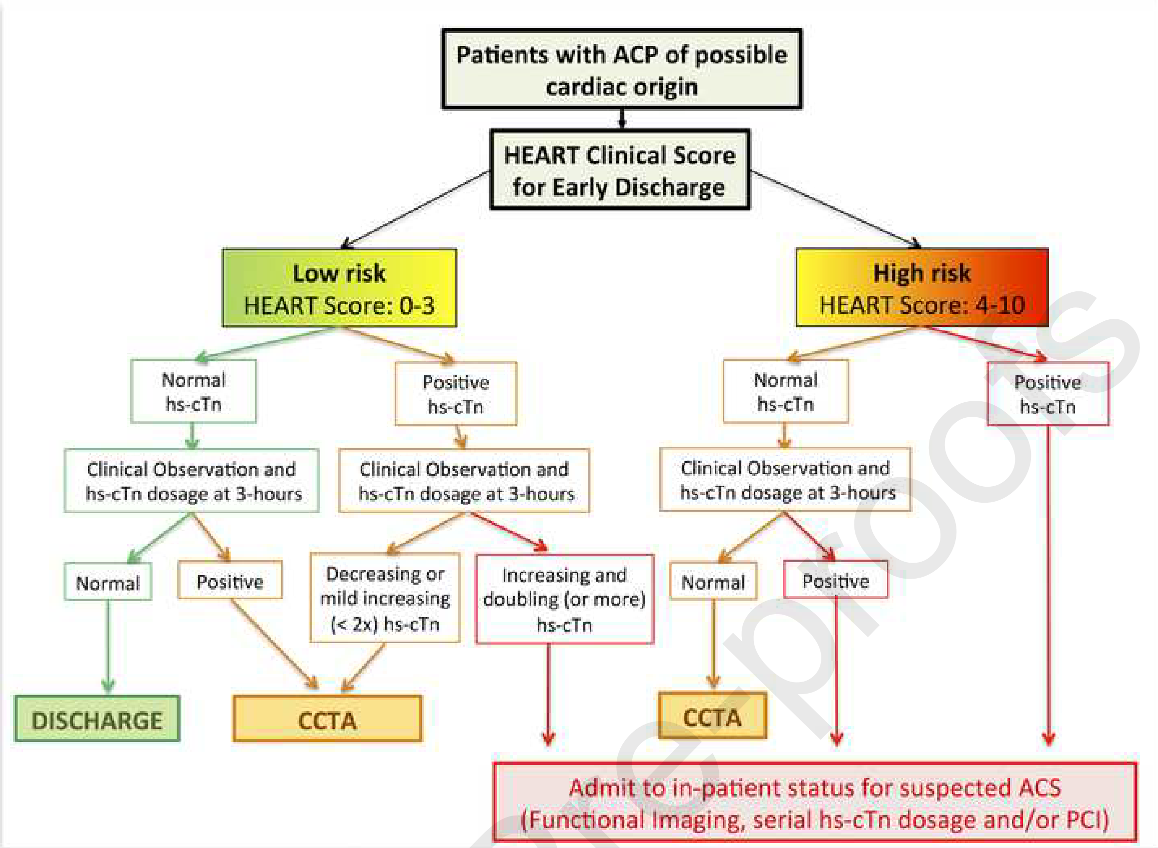
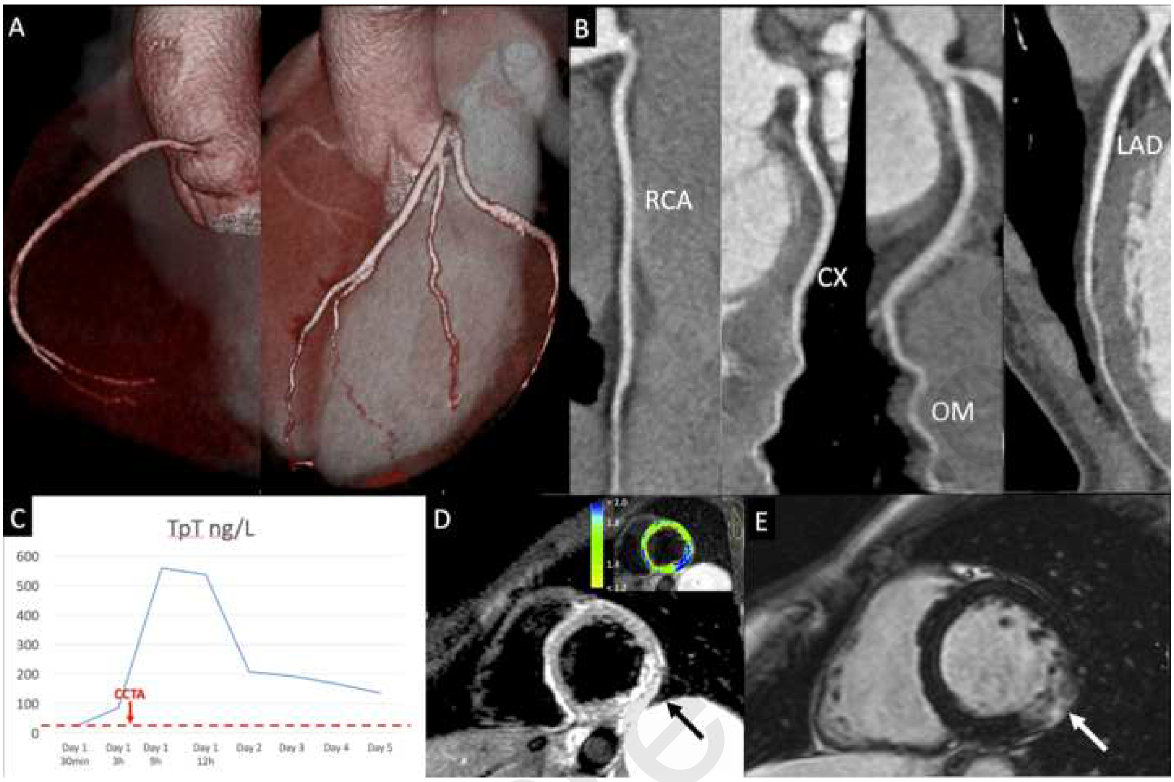
Figure 1



Patients with ACP of possible cardiac origin
HEART Clinical Score for Early Discharge
Low risk
HEART Score: 0-3
High risk
HEART Score: 4-10
Normal hs-cTn
Positive hs-cTn
Normal hs-cTn
Positive hs-cTn
Clinical Observation and hs-cTn dosage at 3-hours
Clinical Observation and hs-cTn dosage at 3-hours
Clinical Observation and hs-cTn dosage at 3-hours
Normal
Positive
Decreasing or mild increasing (< 2x) hs-cTn
Increasing and doubling (or more) hs-cTn
Normal
Positive
DISCHARGE
CCTA
CCTA
Admit to in-patient status for suspected ACS
(Functional Imaging, serial hs-cTn dosage and/or PCI)

Figure 2


A
B
RCA
CX
OM
LAD
C
TpT ng/L
600
500
400
300
200
100
0
CCTA
Day 1 30min
Day 1 3h
Day 1 9h
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Day 2
Day 3
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Day 5
D
E

Figure 3

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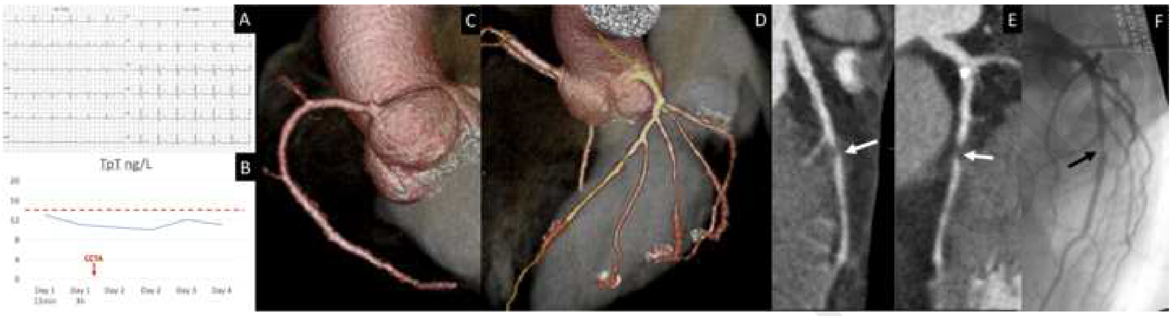
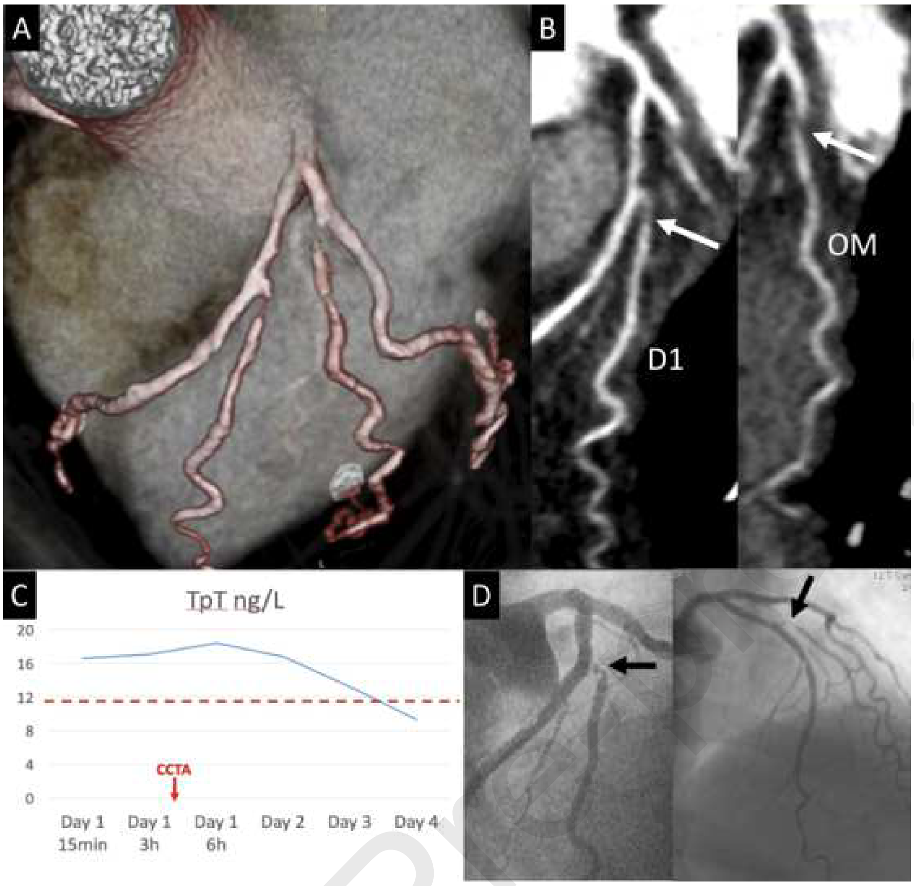


Figure 4


A
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Day 1 15min
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Figure 5

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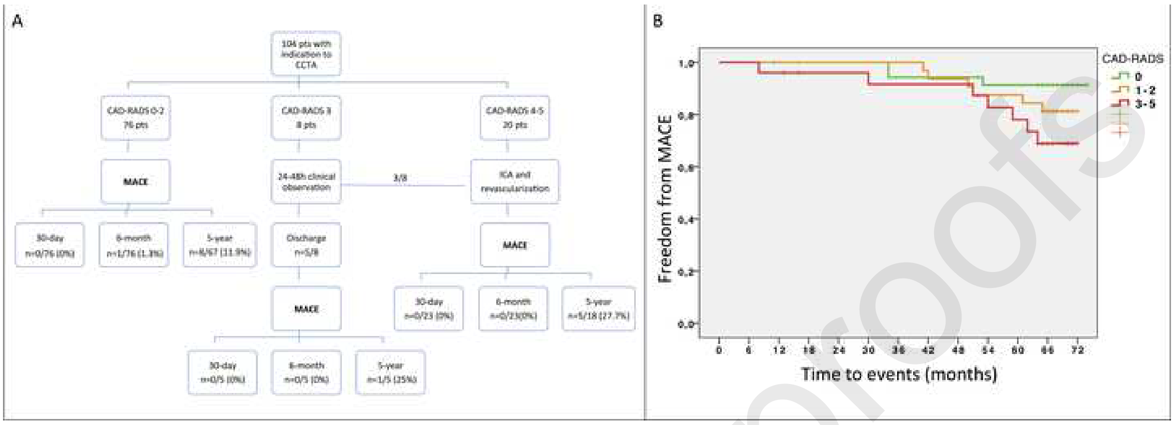

Graphical Abstract