Coronary Computed Tomography Angiography in the Assessment of Acute Chest Pain in the Emergency Room

Carlos Eduardo Elias dos Prazeres[1], Roberto Caldeira Cury[1], Adriano Camargo de Castro Carneiro[1], Carlos Eduardo Rochitte[1,2]

Hospital do Coração - HCor, Associação do Sanatório Sírio[1]; Instituto do Coração - InCor - HCFMUSP[2], São Paulo, SP – Brazil

Abstract

The coronary computed tomography angiography has recently emerged as an accurate diagnostic tool in the evaluation of coronary artery disease, providing diagnostic and prognostic data that correlate directly with the data provided by invasive coronary angiography. The association of recent technological developments has allowed improved temporal resolution and better spatial coverage of the cardiac volume with significant reduction in radiation dose, and with the crucial need for more effective protocols of risk stratification of patients with chest pain in the emergency room, recent evaluation of the computed tomography coronary angiography has been performed in the setting of acute chest pain, as about two thirds of invasive coronary angiographies show no significantly obstructive coronary artery disease. In daily practice, without the use of more efficient technologies, such as coronary angiography by computed tomography, safe and efficient stratification of patients with acute chest pain remains a challenge to the medical team in the emergency room.

Recently, several studies, including three randomized trials, showed favorable results with the use of this technology in the emergency department for patients with low to intermediate likelihood of coronary artery disease. In this review, we show data resulting from coronary angiography by computed tomography in risk stratification of patients with chest pain in the emergency room, its diagnostic value, prognosis and cost-effectiveness and a critical analysis of recently published multicenter studies.

Introduction

This systematic review addresses the current evidence of computed tomography angiography of coronary arteries and the recent impact of almost simultaneous publication of three large controlled, multicenter, randomized studies on the use of this new technology in clinical practice. Clinical and epidemiological importance of coronary artery disease, coronary artery CT angiography technology and its recent evolution, the initial single-center studies, meta-analyses, and finally, randomized trials, a critical analysis of the latter data and recent data on cost effectiveness and clinical impact are reviewed.

The clinical and epidemiological importance of coronary artery disease and acute coronary syndrome

In 2008, the overall rate of deaths attributed to cardiovascular disease (CVD) was 244.8 per 100,000 inhabitants, accounting for 811,940 deaths out of a total of 2,471,984, or one out of every three deaths in the United States. Based on these data, approximately 2,200 Americans die each day in the United States of cardiac causes, or there is one death every 39 seconds. Coronary Artery Disease (CAD) is responsible for almost 50% of these deaths (405,309), with 195,000 cases of acute myocardial infarction, resulting in a coronary event every 25 seconds and approximately one death per minute, despite costs with CVD of $ 297.7 billion, which represents 16% of total health costs, higher than any other group of diseases[1].

As in the United States, cardiovascular disease in Brazil remains the leading cause of death from chronic noncommunicable diseases, although the financial costs are the highest among the disease groups. In spite of a 26% decrease observed in rates of death attributed to cardiovascular causes between 1996 and 2004, Brazil has one of the highest death rates from CVD in South America (286 per 100,000 inhabitants), only exceeded by the rates presented by Guyana and Suriname. Similarly, this group of disease has the highest rates of hospital admissions. In 2007, 12.7% of hospital admissions unrelated to pregnancy and 27.4% of admissions of patients aged > 60 years were due to cardiovascular diseases[2].

Given these alarming numbers, the diagnostic evaluation of patients with acute chest pain is a major challenge in the emergency rooms, both from the standpoint of diagnosis and optimization and adequate targeting of resources. As the Acute Coronary Syndrome (ACS) represents almost one fifth of the causes of chest pain in the emergency rooms and has a high mortality rate, the initial approach of these patients is always done in order to confirm or exclude the diagnosis, seeking to optimize the time to the beginning of treatment or safely discharge them.

Current protocols, however, are not effective in screening this group of patients with acute chest pain of low and intermediate risk, where myocardial necrosis markers are normal and electrocardiographic alterations are absent or nonspecific.

These protocols, until recently, did not include diagnostic tools that provided information on the presence

Keywords

Coronary Artery Disease; Tomography / utilization; Chest Pain; Emergency Service, Hospital.

Mailing Address: Prof. Dr. Carlos Eduardo Rochitte •
Rua Desembargardor Eliseu Guilherme, 123, 3o. Subsolo - Ressonância e Tomografia Cardiovascular, Paraíso, São Paulo - SP - Brazil, Postal Code 04004-030
E-mail: rochitte@cardiol.br, rochitte@incor.usp.br
Manuscript received June 26; 2013, revised manuscript July 01, 2013; accepted July 10, 2013.

DOI: 10.5935/abc.20130208

and severity of CAD. As a result, the confirmation or exclusion of ACS, particularly in patients with unstable angina, required the excessive use of diagnostic tests, resulting in an excess of hospital admissions or possibly in delayed treatment initiation. Thus, the recent introduction of CT coronary artery angiography started a new scenario in the emergency department for evaluation of patients with acute chest pain.

The technology of computed tomography coronary artery angiography: the coronary angiotomography

With the advances in technology over the past decades, since the introduction of electron-beam CT scanner capable of measuring coronary artery calcification to the current tomography equipment with Multi-Detector Computed Tomography (MDCT), the ability to perform cardiac imaging has added significant gain in terms of diagnostic accuracy. Multiple studies have shown that coronary stenoses can be noninvasively identified by computed tomography if high quality images are reproduced.

The quality for cardiac image on CT is directly related to the evolution of CT scanners. The increase in the rotation velocity of the x-ray tubes to less than 500 ms, and increase in the number of detectors from 4 to 64 or more, as well as the decrease in the thickness of the acquired slice to submillimeter levels have brought a significant increase in diagnostic accuracy of coronary artery disease by CT coronary angiography[3], allowing the diagnostic visualization of cardiac structures, and more specifically, the anatomical evaluation of the wall and lumen of the coronary arteries with high sensitivity and specificity, as well as disease extent.

Nevertheless, concerns about patient safety considering radiation exposure has always guided this technology evolution and thus, the latest generation of CT scanners provide optimal image quality with significantly lower radiation doses than the previous ones, reducing exposure by more than 50%.

Thus, the computed tomography of the coronary arteries (CTCor) has become a useful diagnostic tool in the setting of acute chest pain in the emergency room, especially in cases of suspected acute coronary syndrome without ST-elevation, providing high-quality and reproducibility medical information and a new perspective on the diagnosis, prognosis and therapeutic decision.

Controlled studies on coronary CT angiography

Accuracy of coronary CT angiography in CAD - Meta-analyses and Controlled Clinical Trials

Since the introduction of CT scanners with 64 columns of detectors in 2003, more than 50 studies have been published comparing the diagnostic performance of CTCor with the reference standard, the invasive coronary angiography (CA). These studies have shown excellent diagnostic performance per patient, with high sensitivity (S) and specificity (Sp), ranging from 91% to 99% and 74% to 96%, respectively[4-8]. However, the method validation occurred with the publication of three multicenter studies[9-11] designed to assess and detail the diagnostic performance of CTCor in different populations (Table 1).

One of these studies was the ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) study[9], which involved patients without known CAD with stable angina or those alterations in functional tests. The diagnostic performance of CTCor to detect stenosis ≥ 70% when compared to the CA showed S = 94%, Sp = 83%, Positive Predictive Value (PPV) = 48% and Negative Predictive Value (NPV) = 99%, with the area under the ROC curve = 0.95, showing a high diagnostic accuracy to confirm as well as to exclude significant coronary stenosis.

Another multicenter study, the CORE64 (Coronary Evaluation on 64)[10], included 291 patients with and without known CAD with Agatston calcium score < 600, resulting in a higher prevalence of CAD, of 56% threshold of luminal narrowing > 50%. In this study, which was the first and only one to quantitatively measure coronary stenosis by CT angiography, S, Sp, PPV and NPV per patient were 85%, 90%, 91% and 83%, respectively. The findings of lower NPV and PPV were due to a higher prevalence of CAD in this study. The method accuracy, defined as the area under the ROC curve, was 0.91 for CAD confirmed by coronary angiography. Additionally, CTCor was similar to CA when predicting the need for coronary revascularization at the 30-day follow-up.

The European prospective multicenter study evaluated 360 patients without known CAD with acute chest pain and unstable angina[11]. As expected, the prevalence of CAD was high (68%), and the diagnostic performance of CTCor showed S, Sp, PPV and NPV of 99%, 64%, 86% and 97%, respectively. Together, the three multicenter studies showed high sensitivity and NPV in individuals without known CAD, identifying the CTCor capacity to detect and exclude significant coronary stenosis.

Initial studies of coronary CT angiography in ACS - single-center studies and meta-analyses

With the validation of the method, showing its high diagnostic performance, especially its high negative predictive value, plus the absence of a safe and effective protocol for risk stratification in ACS without ST-elevation in groups with low to intermediate risk, studies investigated the inclusion of CTCor into diagnostic research in situations of acute chest pain in emergency rooms.

Meijboom et al[12] evaluated 104 patients presenting with ACS without ST-elevation, classified as high (n = 71) and low risk (n = 33) according to clinical and electrocardiographic criteria and myocardial necrosis markers. Using CA as the reference standard, the diagnostic performance of CTCor in detecting significant coronary lesions (stenosis ≥ 50%) showed S = 100% (88/88, 95% CI: 95 – 100), Sp = 75% (12/16, 95% CI: 47 – 92), PPV = 96% (88/92, 95% CI: 89 – 99) and NPV = 100% (12/12, 95% CI: 70 – 100), showing the high sensitivity of CTCor in detecting significant coronary stenosis,

Table 1 - Diagnostic performance of 64-detector MDCT TCCor through prospective multicenter studies

	CORONARY ARTERY DISEASE									
	n	Prevalence CAD	Stable	Unstable	Unknown CAD	Known CAD	Sens	Specif	PPV	NPV
ACCURACY[9]	230	25%	x		x		95%	83%	64%	99%
CORE 64[10]	291	56%	x		x	x	85%	90%	91%	83%
Meijboom[11]	360	68%	x	x	x		99%	64%	86%	97%

CAD: coronary artery disease; Sens: sensitivity; Specif: specificity; PPV: positive predictive value; NPV: negative predictive value.

as well as excluding the presence of significant CAD in this group of patients with high pretest probability of coronary artery disease.

Similarly, Hoffmann et al[13], in a cohort of 103 patients with acute chest pain in the emergency room, with normal ECG and cardiac enzymes, also found similar results to those above. Of the 103 patients, 14 were diagnosed with ACS (acute myocardial infarction without ST-segment elevation = 5 and unstable angina = 9), and CTCor reached the diagnosis of significant stenosis in five patients diagnosed with AMI without ST-segment elevation. Three other patients underwent coronary angiography due to positive provocative test for ischemia, and, similarly to CA, CTCor showed to be accurate in excluding coronary atherosclerosis. In the remaining patients, CTCor was able to exclude the disease and no significant cardiac events were observed in this subgroup during the follow-up period. Moreover, the presence of CAD on coronary CT angiography added information on ACS prediction using the traditional risk factors.

In the study by Rubinshtein et al[14], of a total of 58 patients, the diagnosis of ACS was confirmed in 20 patients, with CTCor disclosing significant coronary lesions (stenosis ≥ 50%) in 23 subjects, resulting in S = 100%, Sp = 92%, PPV = 87% and NPV = 100%. Of the other 35 patients, 15 showed no CAD and the remaining 20 showed nonobstructive coronary disease. During 15-month follow-up, there was no death or myocardial infarction among the 35 patients in whom CTCor showed no significant stenosis. Thus, the sensitivity of CTCor to predict major cardiovascular outcomes (death, myocardial infarction or revascularization) during hospitalization and 15-month follow-up was 92%, Sp = 76%, PPV = 52% and NPV = 97%.

In another study involving 586 patients with suspected ACS classified as low risk by TIMI (Thrombolysis In Myocardial Infarction) score, a CTCor was promptly performed in 285 patients and after 9 hours, in other 283 patients. In this scenario, the CTCor was able to exclude significant coronary disease in 476 (84%) subjects, who were safely and quickly discharged from the emergency room. None of these patients died or had nonfatal myocardial infarction within 30 days of the examination[15].

Researchers from Seoul National University[16] randomized 268 patients with acute chest pain to undergo CTCor with 64-detector MDCT and reduced the need for hospitalization in the group classified as intermediate risk for CAD, as well as reduced hospital length of stay. At the 30-day follow-up, no patients in the group submitted to CTCor had any major cardiac event, whereas one patient submitted to conventional strategy had an acute myocardial infarction.

Goldstein et al[17] reached the same conclusions in another randomized study. In addition to evaluating the diagnostic efficacy, this study evaluated the method safety and efficiency. CTCor was able to promptly identify and exclude coronary disease as the cause of chest pain in 75% of cases, including 67 patients with normal coronary arteries and 8 patients with significant coronary disease. Regarding safety, when compared to the standard protocol (Myocardial Perfusion Scintigraphy [MPS]), the CTCor was as safe as the scintigraphy. Moreover, the time to diagnosis (3.4 h x 15 h) and costs (U.S.$ 1,586 vs. U.S.$ 1,872) were significantly lower in the group that used the CTCor ($p < 0.001$), also demonstrating that the coronary CT angiography can safely, effectively and efficiently confirm or exclude CAD as the cause of acute chest pain in the emergency room.

Because many institutional protocols use the Exercise Testing (ET) to stratify risk in patients with acute chest pain, the prognostic value of CTCor when compared to ET was evaluated. Of a total of 471 patients, 424 (90%) completed the follow-up of 2.6 years. A total of 44 major cardiac events occurred in 30 patients (4 cardiac deaths, 6 nonfatal myocardial infarctions, 23 revascularizations and 11 episodes of unstable angina). The presence of obstructive CAD was associated with a significantly higher rate of events when compared to the absence of obstructive CAD (6.8% vs. 1.2%, $p < 0.001$).

The results of the ET showed an annual rate of 1.6% events when normal, 1.9% when positive (ET with ischemic response), and 4.6% when inconclusive. A statistically significant increase in the overall risk analysis was detected after adding the findings of CTCor (Chi-square 13.7 *versus* 37.7, $p < 0.001$, respectively). The increase in the resulting net reclassification index (NRI) of the patient was also evaluated, with NRI of 54% with ET (160 patients reclassified as more severe and 249 as less severe) and NRI of 80% with the results of CTCor (132 reclassified as more severe and 277 as less severe).

Thus, the findings of CTCor show to be a strong predictor of future cardiac events, demonstrating incremental value over the clinical and exercise test findings[18].

The ROMICAT[19] study showed that in a population with low to intermediate risk for ACS with acute chest pain, 50% had no coronary lesions at the CTCor. In this study, CTCor

showed a diagnostic performance of S = 100%, Sp = 54%, PPV = 17%, NPV = 100% for the evaluation of presence of any coronary atherosclerotic plaque. When analyzing the presence of obstructive CAD (≥ 50% luminal narrowing), S was 77%, Sp = 87%, PPV = 35% and NPV = 98%. Both the presence of CAD and of significant stenosis were able to predict ACS at the CTCor regardless of risk factors or TIMI score. Through these findings, given the large number of patients with acute chest pain, the early performance of CTCor substantially improved the therapeutic management in this group of patients by enabling an earlier clinical decision, more effectively targeting the treatment or safely allowing hospital discharge and reducing unnecessary hospitalizations.

These same investigators, after a two-year follow-up, published the prognostic results of the ROMICAT study. Of the 368 patients, 333 (90.5%) completed the follow-up. Thirty-five events were observed in 25 (6.8%) patients (12 AMI and 23 revascularizations). The cumulative probability of major cardiac outcomes (MACE) increased with the degree of coronary artery disease (no CAD = 0%, nonobstructive CAD = 4.6% and obstructive CAD = 30.3%, $p < 0.0001$), as well as when associating the degree of CAD to left ventricular segmental dysfunction (LVSD), evidenced by MDCT (without stenosis or LVSD = 0.9%; one finding: LVSD = 15% or stenosis = 10.1%, both present = 62.4%, $p < 0.0001$).

The C statistical test to predict MACE was 0.61 according to the TIMI score and increased to 0.84 by adding the degree of the CAD at the CTCor and to 0.91 by adding the degree of CAD and LVSD. From this study it can be concluded that among patients who come to the emergency room with acute chest pain and low to intermediate risk of ACS, the absence of CAD at the CTCor predicts a period free of cardiac events of two years, while the presence of coronary stenosis with LVSD is associated with high probability of MACE in the same period[20]. Similar results were found by Chow et al[21], who showed prognostic and incremental value of CAD severity, left ventricular ejection fraction and total CAD burden as detected by CTCor over classical clinical predictors.

A recent meta-analysis published in 2010 that included 16 studies, some of which are listed here, with a total of 1,119 patients, showed S = 96% (95% CI, 93-98%), Sp = 92% (95% CI, 89-93%) and ROC curve of 0.98, also demonstrating the high value of coronary CT angiography for the diagnosis of significant coronary stenosis in the presence of acute chest pain. However, S and Sp are associated only to the test and not to the practical use to estimate disease likelihood in the individual scenario. The likelihood ratio (LR), in turn, is the chance that a positive test is a true positive and a negative test is a false negative. These last tests, therefore, provide a better understanding of the suspected disease.

A good diagnostic test, consequently, has a high LR for a positive test and a low LR for the negative test. The CTCor in this analysis showed a positive LR of 10.12 and negative LR of 0.09. A value greater than 10 for positive LR provides strong evidence to confirm the diagnosis, virtually conclusive. Similarly, a very low value for negative LR, of 0.09, virtually ruled out the possibility that the cause of the chest pain is due to significant coronary disease[22].

Recent randomized clinical trials in ACS

Considering the results obtained by the single-center studies, randomized multicenter trials were designed to confirm the previous results at a better level of evidence. With the publication of three multicenter trials: CT-STAT[23], ACRIN PA[24] and ROMICAT II[25], which showed results consistent with each other, the use of coronary CT angiography in the presence of acute chest pain, applied to the appropriate population, reached the criterion for Class I indication with level of evidence A (Table 2).

The "Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment (CT-STAT)" study involved 16 centers and a total of 699 patients, of which 361 underwent CTCor and 338 MPS. With the primary goal of diagnostic efficiency (time to diagnosis), patients in the CTCor group had a reduction of 54% in that time (2.9 h x 6.3 h, $p < 0.0001$) compared to standard protocol with MPS. The costs involved and safety were the secondary endpoints. With respect to costs, these also were lower among patients using CT angiography, with a reduction of 38% ($ 2,137 x $ 3,458, $p < 0.0001$). The diagnostic strategies did not differ in the rate of major cardiac events (0, 8% vs. 0.4%, $p = 0.29$) during the mean follow-up of six months. Therefore, this study showed that among patients with acute chest pain of low risk the use CTCor resulted in earlier diagnosis, at a lower cost than the MPS and with the same degree of safety[23].

The ACRIN PA[24] study involved 1,370 patients at low to intermediate risk in five centers in the United States, having as the primary objective the safety profile (events after discharge). This study showed that among patients submitted to CTCor, 640 (83%) did not have CAD, which allowed them to be discharged directly from the emergency room, compared to the standard protocol (49.6% vs. 22.7%, 95% CI: 21.4 to 32.2), resulting in a significant reduction in hospital length of stay (12.3 h vs. 24.7 h, $p < 0.001$). The primary safety endpoint was also demonstrated, as no patient with negative coronary CT angiography had myocardial infarction or cardiac death within 30 days of the examination. Thus, the diagnostic strategy using CTCor as the first imaging examination in the emergency department for patients with low to intermediate risk allowed them to be safely discharged after negative testing, increasing medical discharge rates and decreasing hospital length of stay[24].

The most recent study, ROMICAT II[25], had as primary objective to assess the length of hospital stay (from arrival at the emergency room until discharge), as it reflects clinical information (diagnosis and treatment) and issues of costs and logistics of the involved centers. Among the thousand patients enrolled, 501 were randomized to the CTCor, and 499 patients were randomized to the standard treatment group, which consisted in following the chest pain protocols that were specific for the routine of the involved institutions (serial evaluation of myocardial necrosis markers, electrocardiogram and other diagnostic tests other than CTCor or intervention, according to medical indication).

Table 2 - The three multicenter, randomized controlled trials that evaluated the performance of TCCor in the setting of acute chest pain in the emergency room

	Number of Centers	n (randomization)	TIMI score	Time (h)*	30-day events‡	Cost ($)§
CT-STAT[23]	16	699 (1:1)	0-4	2.9 vs. 6.3*, †	0.8 vs. 0.4‡	2137 vs. 3458§
ACRIN-PA[24]	5	1370 (2:1)	0-2	18 vs. 24.8*	zero	NA
ROMICAT II[25]	9	985 (1:1)	Low risk/ intermediate risk	23 vs. 30.8*	0.4 vs. 1.2‡	2101 vs. 2566§

*n: number of patients involved in the study; TIMI: thrombolysis in myocardial infarction. * p < 0.0001. †CT-STAT time refers to the time until the diagnosis; The 30-day event rate was not statistically significant between groups; § The difference in costs was statistically significant between groups.*

When compared with the patients randomized to the group submitted to the standard protocol, patients undergoing CTCor had a significant reduction of 7.6 h ($p < 0.001$) in the length of hospital stay. Within 8.6 h of arrival at the emergency, 50% of patients in the CTCor group had been discharged, compared to only 10% of the group submitted to the standard protocol. The time to reach a diagnosis, even in the subgroup with a final diagnosis of ACS was significantly lower in the CTCor group than in the standard protocol group (10.4 h x 18.7 h and 10.6 h x 18.8 h, respectively). Similarly, during the 28-day follow-up, the rate of events (secondary objective) was infrequent. Six events occurred in the standard protocol group, whereas in the CTCor group there were two events. In these two events that occurred in the CTCor group, the tomography assessment showed significant coronary lesion (stenosis > 50%), but with a functional negative test, and thus, clinical treatment was initially chosen.

Critical analysis of multicenter studies

The aforementioned scientific evidence provides subsidies for the indication of CTCor use to assess patients with acute chest pain. Figures 1 and 2 show two cases of chest pain in the emergency room; Figure 1 shows a case with bulky plaque and critical proximal stenosis of the ADA, and figure 2 shows a case with myocardial bridge and a mild mixed plaque proximal to the myocardial bridge, which does not cause significant stenosis of the ADA lumen. It should be observed that although clinical symptoms, age and presentation at the emergency room are similar, only the first patient benefited from catheterization procedure. However, patient selection is the key to good diagnostic performance and therapeutic success of chest pain evaluation protocols. In the three multicenter studies, of the patients included, about 50% were females with a mean age of 50 years, which significantly reduces the pre-test probability in this studied population.

Another important question to be asked is whether in fact there is a need to perform additional diagnostic tests before hospital discharge in low-risk patients. The rationale for performing any examination is whether, when compared to a control group, this examination will result in outcome improvement. In the multicenter studies shown here there was no evidence that the performance of the CTCor reduced the incidence of infarctions or deaths. In fact, the rate of major cardiac events among all patients involved in the studies was very low, making it impossible to know whether the CTCor brought any benefit.

Regarding costs, in the CT-STAT study, the investigation protocol in which the CT angiography showed stenosis between 25% and 70%, the patients were also submitted to the MPS. Therefore, further tests were generated and the costs increased in the CTCor group, as lesions between 25% and 49% are not considered significant, as shown by the results of the 37 patients from the CTCor group submitted to MPS, of which 30 (81%) had normal functional test.

In the ROMICAT II study, it is emphasized that even before a more efficient screening, this gain was not achieved under the risk of misdiagnosis. In that study, there were no cases reported in either group, indicating that the higher number of early discharges from the emergency department with the use of coronary CT angiography did not result in misdiagnosis, demonstrating the method safety. In the same study, however, the results showed that patients undergoing CTCor generated the use of more diagnostic resources, findings also described by Shreibati et al[26], but not observed in the CT-STAT study[23]. However, when considering the final costs, the mean costs of the index visit and at the end of the 28-day follow-up were similar in the CTCor group and standard protocol group ($p = 0.65$).

Therefore, protocols that use of coronary CT angiography as the initial imaging test in the management of patients with acute chest pain and possible ACS, reduce the length of hospital stay, attain an earlier diagnosis, increase efficiency in medical decision-making in the emergency room, without generating an increase in the total costs and without the risk of discharging patients with ACS (probability less than 1% in the three multicenter trials).

Coronary CT angiography and cost effectiveness

Despite all the advantages demonstrated, for a method to be incorporated into the diagnostic routine, it must be cost-effective, in addition to showing accurate diagnostic performance.

In a recent multicenter study aimed to total health care costs and the related CAD in 8,235 low-risk patients undergoing CTCor and MPS, the costs at the end of one year were 25.9% lower in subjects undergoing CTCor compared with those who underwent MPS, with an average of $ 1,075 per patient[27]. This difference was mainly due to a lesser

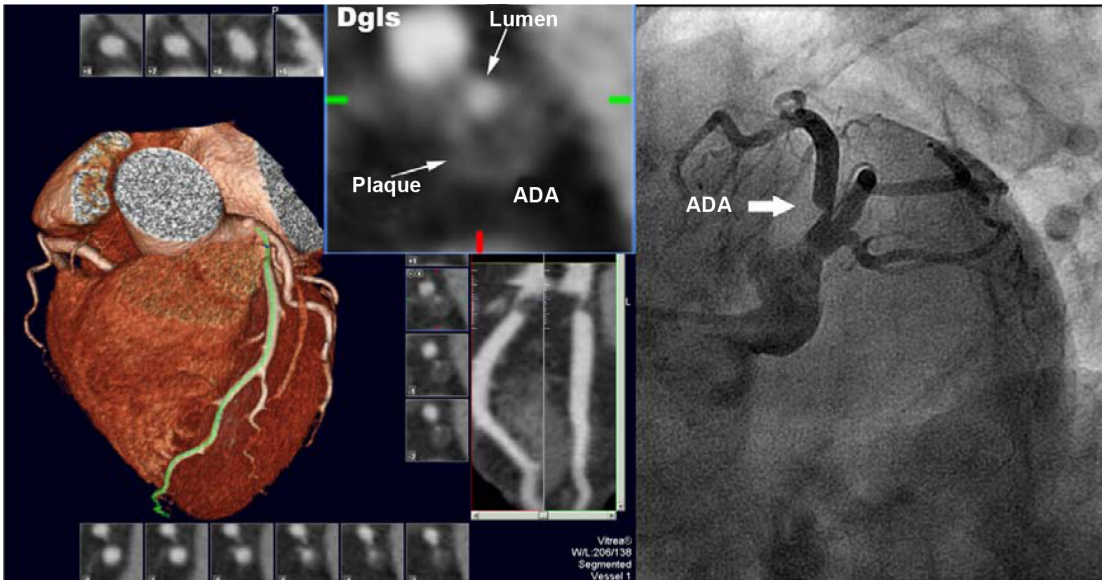

Figure 1 - *65-year-old male patient that came to the emergency room with atypical chest pain, nonspecific ECG and normal myocardial necrosis markers (enzymes).*

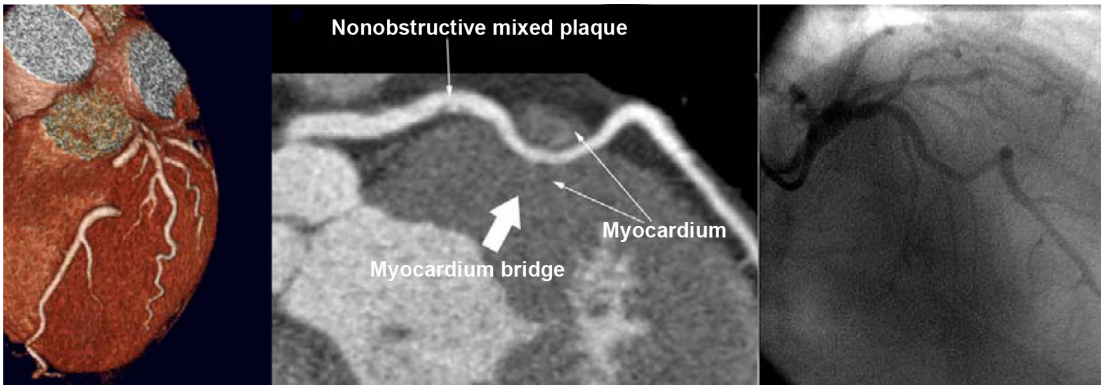

Figure 2 - *61-year-old male patient presenting to the emergency department with atypical chest pain, nonspecific ECG and normal myocardial necrosis markers (enzymes).*

need for invasive examination and revascularization among patients undergoing coronary CT angiography.

These findings can be extended to a similar study with 9,690 intermediate-risk individuals also submitted to CTCor or MPS[28]. In a nine-month follow-up, the costs related to CAD were one-third lower for patients undergoing CTCor, with an average of $ 467 per patient. The cost related to medication and the need for revascularization was similar between the groups and the difference was due to the need for additional diagnostic tests among patients undergoing MPS, especially CA.

In 2011, Miller et al. added CTCor to the standard protocol in the risk stratification of patients with acute chest pain in the emergency room and randomized resource utilization with the standard protocol. A total of 60 patients were enrolled in this study. The total amount of resources used in CTCor group in up to 90 days of follow-up was $ 10,134 vs. $ 16,579 in the standard group. By using this additional resource, in addition to reduction in total costs, there were fewer hospital readmissions (6/30 vs. 16/30, p = 0.007) and greater diagnostic power of CAD (19 patients were diagnosed with CAD, of which 18 (95%) belonged to the CTCor group)[29].

Clinical impact of new evidence

As almost about 10% of stress tests are inconclusive leading to coronary angiography, and these are negative in the majority of cases, the ACIC study evaluated the correlation between stress testing (MPS, ET and stress echocardiography) with CTCor, and compared the diagnostic performance with CA in 47 centers. Of a total of 6,198 patients, 1,548 (24.9%) had normal tests, 1,027 (16.6%) were inconclusive and 3,623 (58.5%) were positive. In the multivariate analysis, the result of the stress test did not bring incremental value over the Framingham risk score. Overall S, Sp, PPV and NPV of the stress testing was 60.4%, 34.2%, 59.3% and 35.2%, respectively.

The diagnostic performance for stenosis ≥ 50% of the CTCor was S = 93.7%, Sp = 37.9%, PPV = 70.6% and NPV = 79.1%. The association between the CTCor and CA findings was statistically significant (OR: 9.1, 95% CI: 5.57 to 14.81, $p < 0.001$), while results from stress testing and coronary angiography showed no association (OR: 0.79, 95% CI: 0.56 to 1.11, $p = 0.17$). Thus, the degree of stenosis in CTCor was the strongest additional predictor of significant coronary lesion in CA, with the results of the stress test having no incremental value over the clinical variables[30].

In a recent publication of the CONFIRM registry, the use of CTCor showed to be a cost-effective diagnostic tool in CAD investigation. With approximately 15,000 patients included, of which 56.4% of patients had typical and atypical chest pain, CA rates were very low in patients without CAD or with mild CAD detected by CTCor, showing that in real life doctors are accepting the results obtained by CTCor, in this case, its high negative predictive value. Nevertheless, these same patients showed no increase in the rates of major cardiac events, confirming the examination safety.

Similarly, of the patients submitted to invasive angiography after undergoing CTCor, the rate of percutaneous revascularization was directly related to the degree of coronary artery disease detected by CT, increasing from 2% to 28.5% for those with mild disease and obstructive disease respectively, as well as for surgical revascularization. Thus, this registry, which translates real-life medical practice, clarifies that the inclusion of CTCor into routine practice does not translate into increased resource utilization and therefore, costs. Rather, there was a reduction in the procedures, particularly high-cost ones, showing to be a highly effective and safe examination in the screening of patients for atherosclerosis investigation[31].

Conclusion

In the setting of acute chest pain, the use of CT coronary angiography in groups of low to intermediate risk has shown to be an efficient, effective and safe method, with significant prognostic value, reducing costs and hospitalization time and optimizing treatment in emergency rooms.

Author contributions

Conception and design of the research and Writing of the manuscript: dos Prazeres CEE, Cury RC, Carneiro ACC, Rochitte CE; Acquisition of data and Statistical analysis: dos Prazeres CEE, Rochitte CE; Analysis and interpretation of the data: dos Prazeres CEE, Carneiro ACC, Rochitte CE; Critical revision of the manuscript for intellectual content: Cury RC, Carneiro ACC, Rochitte CE.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

References

1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation. 2012;125(1):188-97. Erratum in: Circulation. 2012;125(22):e1001.
2. Schmidt MI, Duncan BB, Azevedo e Silva G, Menezes AM, Monteiro CA, Barreto SM, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. Lancet. 2011;377(9781):1949-61.
3. Cordeiro MA, Lima JA. Atherosclerotic plaque characterization by multidetector row computed tomography angiography. J Am Coll Cardiol. 2006;47(8 Suppl):C40-7.
4. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E, Kober L, Torp-Pedersen C. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. Eur Heart J. 2007;28(24):3042-50.
5. Mowatt G, Cook JA, Hillis GS, Walker S, Fraser C, Jia X, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. Heart. 2008;94(11):1386-93.
6. Mowatt G, Cummins E, Waugh N, Walker S, Cook J, Jia X, et al. Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease. Health Technol Assess. 2008;12(17):iii-iv, ix-143.
7. Hamon M, Biondi-Zoccai GG, Malagutti P, Agostoni P, Morello R, Valgimigli M, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a meta-analysis. J Am Coll Cardiol. 2006;48(9):1896-910.
8. Hamon M, Morello R, Riddell JW. Coronary arteries: diagnostic performance of 16- versus 64-section spiral CT compared with invasive coronary angiography-meta-analysis. Radiology. 2007;245(3):720-31.

9. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol. 2008;52(21):1724-32.

10. Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, et al. Diagnostic performance of coronary angiography by 64-row CT. N Engl J Med. 2008;359(22):2324-36.

11. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. J Am Coll Cardiol. 2008;52(25):2135-44.

12. Meijboom WB, Mollet NR, Van Mieghem CA, Weustink AC, Pugliese F, van Pelt N, et al. 64-Slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart. 2007;93(11):1386-92.

13. Hoffmann U, Nagurney JT, Moselewski F, Pena A, Ferencik M, Chae CU, et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. Circulation. 2006;114(21):2251-60. Erratum in: Circulation. 2006;114(25):e651.

14. Rubinshtein R, Halon DA, Gaspar T, Jaffe R, Karkabi B, Flugelman MY, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation. 2007;115(13):1762-8.

15. Hollander JE, Chang AM, Shofer FS, McCusker CM, Baxt WG, Litt HI. Coronary computed tomographic angiography for rapid discharge of low-risk patients with potential acute coronary syndromes. Ann Emerg Med. 2009;53(3):295-304.

16. Chang SA, Choi SI, Choi EK, Kim HK, Jung JW, Chun EJ, et al. Usefulness of 64-slice multidetector computed tomography as an initial diagnostic approach in patients with acute chest pain. Am Heart J. 2008;156(2):375-83.

17. Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol. 2007;49(8):863-71.

18. Dedic A, Genders TS, Ferket BS, Galema TW, Mollet NR, Moelker A, et al. Stable angina pectoris: head-to-head comparison of prognostic value of cardiac CT and exercise testing. Radiology. 2011;261(2):428-36.

19. Hoffmann U, Bamberg F, Chae CU, Nichols JH, Rogers IS, Seneviratne SK, et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. J Am Coll Cardiol. 2009;53(18):1642-50.

20. Schlett CL, Banerji D, Siegel E, Bamberg F, Lehman SJ, Ferencik M, et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-year outcomes of the ROMICAT trial. JACC Cardiovasc Imaging. 2011;4(5):481-91.

21. Chow BJ, Wells GA, Chen L, Yam Y, Galiwango P, Abraham A, et al. Prognostic value of 64-slice cardiac computed tomography severity of coronary artery disease, coronary atherosclerosis, and left ventricular ejection fraction. J Am Coll Cardiol. 2010;55(10):1017-28.

22. Athappan G, Habib M, Ponniah T, Jeyaseelan L. Multi-detector computerized tomography angiography for evaluation of acute chest pain--a meta analysis and systematic review of literature. Int J Cardiol. 2010;141(2):132-40.

23. Goldstein JA, Chinnaiyan KM, Abidov A, Achenbach S, Berman DS, Hayes SW, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. 2011;58(14):1414-22.

24. Litt HI, Gatsonis C, Snyder B, Singh H, Miller CD, Entrikin DW, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. N Engl J Med. 2012;366(15):1393-403.

25. Hoffmann U, Truong QA, Schoenfeld DA, Chou ET, Woodard PK, Nagurney JT, et al; ROMICAT-II Investigators. Coronary CT angiography versus standard evaluation in acute chest pain. N Engl J Med. 2012;367(4):299-308.

26. Shreibati JB, Baker LC, Hlatky MA. Association of coronary CT angiography or stress testing with subsequent utilization and spending among Medicare beneficiaries. JAMA. 2011;306(19):2128-36.

27. Min JK, Kang N, Shaw LJ, Devereux RB, Robinson M, Lin F, et al. Costs and clinical outcomes after coronary multidetector CT angiography in patients without known coronary artery disease: comparison to myocardial perfusion SPECT. Radiology. 2008;249(1):62-70.

28. Min JK, Shaw LJ, Berman DS, Gilmore A, Kang N. Costs and clinical outcomes in individuals without known coronary artery disease undergoing coronary computed tomographic angiography from an analysis of Medicare category III transaction codes. Am J Cardiol. 2008;102(6):672-8.

29. Miller AH, Pepe PE, Peshock R, Bhore R, Yancy CC, Xuan L, et al. Is coronary computed tomography angiography a resource sparing strategy in the risk stratification and evaluation of acute chest pain? Results of a randomized controlled trial. Acad Emerg Med. 2011;18(5):458-67.

30. Chinnaiyan KM, Raff GL, Goraya T, Ananthasubramaniam K, Gallagher MJ, Abidov A, et al. Coronary computed tomography angiography after stress testing: results from a multicenter, statewide registry, ACIC (Advanced Cardiovascular Imaging Consortium). J Am Coll Cardiol. 2012;59(7):688-95.

31. Shaw LJ, Hausleiter J, Achenbach S, Al-Mallah M, Berman DS, Budoff MJ, et al; CONFIRM Registry Investigators. Coronary computed tomographic angiography as a gatekeeper to invasive diagnostic and surgical procedures: results from the multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry. J Am Coll Cardiol. 2012;60(20):2103-14.