Computer-aided analysis of 64-slice coronary computed tomography angiography: a comparison with manual interpretation

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Abstract

Coronary computed tomography angiography (CCTA) is increasingly used for the assessment of coronary heart disease (CHD) in symptomatic patients. Software applications have recently been developed to facilitate efficient and accurate analysis of CCTA. This study aimed to evaluate the clinical application of computer-aided diagnosis (CAD) software for the detection of significant coronary stenosis on CCTA in populations with low (8%), moderate (13%), and high (27%) CHD prevalence. A total of 341 consecutive patients underwent 64-slice CCTA at 3 clinical sites in the United States. CAD software performed automatic detection of significant coronary lesions (>50% stenosis). CAD results were then compared to the consensus manual interpretation of 2 imaging experts. Data analysis was conducted for each patient and segment. The CAD had 100% sensitivity per patient across all 3 clinical sites. Specificity in the low, moderate, and high CHD prevalence populations was 64%, 41%, and 38%, respectively. The negative predictive value at the 3 clinical sites was 100%. The positive predictive value was 22%, 21%, and 38% for the low, moderate, and high CHD prevalence populations, respectively. This study demonstrates the utility of CAD software in 3 distinct clinical settings. In a low-prevalence population, such as seen in the emergency department, CAD can be used as a Computer-Aided Simple Triage tool to assist in diagnostic delineation of acute chest pain. In a higher prevalence population, CAD software is useful as an adjunct for both the experienced and inexperienced reader.

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Introduction

Coronary computed tomography angiography (CCTA) is increasingly used for the non-invasive assessment of coronary artery disease in stable symptomatic patients. Several multicenter clinical trials comparing 64-slice CCTA with invasive catheter-based coronary angiography have shown remarkable diagnostic accuracy for the detection of obstructive coronary heart disease (CHD) (>50% stenosis).1-2 In addition, a negative CCTA has been demonstrated in multiple studies to improve diagnostic certainty for ruling out significant coronary artery disease in a low-risk acute chest pain population, as well as reduce hospital length of stay and healthcare costs when compared with the standard of care.3,4

The increased utilization of CCTA has resulted in a need to rapidly interpret a large volume of images in an accurate and efficient manner. To meet this growing demand for expert image interpretation, computer-aided diagnosis (CAD) software applications have been developed to expedite the evaluation of coronary heart disease with CCTA. The multiple benefits of automated software programs have been previously demonstrated in many non-cardiac diagnostic imaging modalities.5-7 However, the clinical utility of CAD for the assessment of CHD is still in its infancy. While various software applications have been validated for the automated evaluation of CCTA and automated aortic calcium scoring, a useful commercially available product has yet to be established.8,9

Here we evaluate a dedicated CAD software designed for the automated evaluation of CCTA: the COR Analyzer by Rcadia Medical Imaging. Recently, 3 studies were published which evaluated the COR Analyzer performance and reported promising system sensitivity and negative predictive values.10-12 Furthermore, the 3 studies proved to have specificities of over 60%, which is significant when considering the potential for the software to be used as a Computer-Aided Simple Triage (CAST) tool.13 A successful CAST tool can be employed in the emergency department as an initial rapid read to allow for triage of patients. This is a step forward from the typical CAD role as a confirmatory second reader. However, the past studies evaluating the COR Analyzer were limited in their size as well as in their patient populations and further confirmation of these results is necessary.

The current study aims to further evaluate the applicability of CAD software for the detection of significant coronary stenosis by 64-slice CCTA. We aimed to determine the utility and accuracy of the COR Analyzer compared to
手动CTA分析在各种临床环境中使用不同类型的设备（CT扫描仪）并在不同人群中使用CHD流行率。

**Materials and Methods**

冠状动脉CTA在连续的患者中进行了三次临床试验。在实验中，CTA研究被移交给一个单独的工作站，获得了三个64探测器多探测器CT扫描仪：64探测器Lightspeed VCT扫描仪（GE Healthcare, Milwaukee, Wisconsin）；64探测器Sensation 64 scanner（Siemens Health Care, Forchheim, Germany）；64探测器Aquilion-64 scanner（Toshiba Medical, Tochigi, Japan）。在实验中，将冠状动脉疾病按其血管段进行了分类。直径小于1 mm的血管段被排除。所有CTA研究均包括在最终分析中，除非研究质量或未相关的软件错误导致血管段分析。

在使用冠状动脉CTA时，CAD系统会报告广泛的和阻塞性的疾病。图1显示了正常和阻塞性的CTA读取。

在CTA读取中，CAD系统可能会报告一个警告。在正性研究中，当系统错误时，读者应该检测到一个病变。在负性研究中，人类观察者应该确认没有发现而声明它是负性的。警告不是对用户的跟踪。警告不是对用户邀请额外注意的信号。在实验中，CAD系统可能会报告一个警告，当在自动分析中存在误差或系统不自信时。

结果

总共341名患者符合64-slice CTA在3个临床站点的指示条件。
the United States were included in the study. Of these, 96 patients underwent CCTA in the emergency room (ER) of a suburban tertiary medical center, 196 patients were scanned in a suburban outpatient cardiac imaging center (IC), and 49 patients had CCTA at an urban outpatient cardiology office (OP). The prevalence of CHD (>50% stenosis in one or more vessels) in the population at these 3 locations was low (8%), moderate (13%), and high (27%) for ER, IC, and OP, respectively. Two of the 341 CCTAs were characterized as suboptimal in quality, but were still included in the analysis.

The CAD results categorized the CCTA as positive for obstructive CHD in 37 of the 96 scans performed at ER, 122 of the 196 at IC, and 34 of the 49 in OP. In the segmental analysis, segments were classified as positive in 77 of 960 ER segments, 278 of the 1960 IC segments and 76 of 490 OP segments. The consensus manual interpretation found that 8 of the 96 CCTAs at ER, 26 of the 196 CCTAs at IC, and 13 of the 49 CCTAs at OP had findings consistent with obstructive CHD. On a per segment basis, 19 out of the 960 ER segments, 29 out of the 1960 IC segments, and 27 out of the 490 OP segments were found to be representative of significant coronary stenosis. In the per patient analysis, there were 7 warnings on negative studies in both the ER and IC sites and 0 warnings on negative in the OP site. In the per vessel analysis, there were 24 warnings on negative studies in the ER site, 20 in the IC site, and 6 in the OP site (Table 1).

The CAD had a per patient sensitivity of 100% across all 3 clinical sites. Specificity in the low, moderate, and high CHD prevalence populations was 64%, 41%, and 38%, respectively. The negative predictive value (NPV) at the 3 clinical sites was 100% (this is by default when a test results in a sensitivity of 100% and a specificity >0%). The positive predictive value (PPV) was 22%, 21%, and 38% for the low, moderate, and high CHD prevalence populations, respectively (Table 2). The segmental analysis yielded results with a similar trend (Table 3); however, the absolute values were lower due to misclassification in predominantly distal segments and segments affected by significant motion artifact.

### Discussion

With the introduction of CCTA computer-aided detection software for the automatic detection of significant coronary heart disease, the potential for rapid discharge of patients who present to the emergency department with acute non-myocardial infarction (MI) chest pain is promising. Due to the low-risk nature of the acute non-MI chest pain patient, patients often endure long waiting times for various diagnostic procedures only to have a normal result. Computer-aided detection of CHD in the emergency setting has the potential to efficiently rule out CHD in acute non-MI chest pain patients, and thus can expedite the discharge of a large portion of patients who are in fact negative for CHD. While studies have validated the potential for CAD software for evaluation of CHD, to date, few studies have explored commercially available CAD software.

A past study evaluating the diagnostic accuracy of the COR Analyzer software by comparison with quantitative angiography (QCA) reported a high sensitivity and negative predictive value. However, this study was limited by its small population (n=59) which was restricted to patients referred for QCA; thus, low- to intermediate-risk patients were not assessed. Additionally, a recent mid-sized, 2-center study and a large single center study compared the accuracy of the COR Analyzer software on 64-slice and 256-slice CCTA by comparison with manual interpretation of CCTA, again demonstrated a high sensitivity and negative predictive value. These 3 studies compliment the current, so far largest, multicenter comparison of the CCTA on 64-slice CCTA compared to manual CCTA interpretation.

The present study illustrates that the CAD system can identify abnormal coronary segments when employed in 3 distinct clinical sites with varying incidences of CHD. There was good correlation between manual interpretation and CAD results for the exclusion of significant coronary stenosis.

### Table 1. Warnings on negative for each site, in both the per patient and the per vessel analysis.

| Coronary artery disease prevalence (%) | Low (8%) | Moderate (13%) | High (27%) |
|----------------------------------------|----------|----------------|------------|
| Emergency room                          | 7/96     | 7/196          | 0/49       |
| Outpatient office                       | 24/960   | 20/1960        | 6/490      |

### Table 2. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the identification of significant stenosis (>50%) on coronary computed tomography angiography by computer-aided analysis when compared with manual visual interpretation on a per patient analysis in 3 populations of varying disease prevalence.

| Coronary artery disease prevalence (%) | Low (8%) | Moderate (13%) | High (27%) |
|----------------------------------------|----------|----------------|------------|
| Emergency room                          | 100% (8/8) | 100% (26/26)   | 100% (13/13) |
| Outpatient office                       | 64.2% (52/81) | 41.1% (67/163) | 38.2% (13/34) |
| PPV                                    | 21.6% (8/37) | 21.3% (24/122) | 38.2% (13/34) |
| NPV                                    | 100% (52/52) | 100% (67/67)   | 100% (13/13) |

PPV: positive predictive value; NPV: negative predictive value.
significant CHD across a spectrum of disease prevalence. Specifically there were no false negatives in any of the populations studied.

While the high sensitivity and negative predicative value for CAD using CCTA is promising, both the specificity and positive predicative value were rather low by human analysis standards. On the other hand, when comparing to other known computer-aided analysis systems (e.g. for mammography, colonoscopy, lung nodules, chest X rays, etc.), the reported specificity and PPV (especially in the low-risk population, 8% prevalence) is extremely high. All other computer-aided diagnosis systems available today generate several false alarms on average per every case, yielding a close to zero per patient specificity and PPV.

The system reported in this study, yielding a 64% specificity for a low-risk population, falls into a different category of computer-aided analysis tools: the Computer-Aided Simple Triage (CAST) recently introduced by Goldenberg and Peled. As a CAST tool, it can be used for chest pain patient triage in the emergency department or for reading sequence prioritization in high-volume practices with low-risk populations. For moderate- and high-risk populations, the CAD system yielded lower specificities and cannot, therefore, be used as a CAST in these groups. However, a CAST tool is most useful in the setting of the emergency department where rapid triage of patients is critical, and it is well documented that emergency departments are a low-risk population with regards to coronary artery disease. Therefore, CAD has the potential to significantly aid the experienced practitioner with accurate and efficient CCTA interpretations and maintain throughput, especially in high-volume emergency departments where a rapid evaluation for CHD is crucial. A recent study using the COR Analyzer software supports the current study’s results in the low-risk population, demonstrating a 63% specificity, further supporting the usage of the COR Analyzer software as a potential CAST tool.

Although the evaluated CAD system cannot be used as a CAST tool for moderate- (13% prevalence) and high-risk (27% prevalence) populations due to the subpar specificities and PPV, it still has a role in these categories of patients. In populations in which false positives are common, inexperienced radiologists can still benefit from having the second reader. Furthermore, it is important to note that the experienced reader can also benefit from the CAD software in populations where false positives reads by the CAD software are frequent. Every study reported as positive by the computer system is to be immediately reviewed by a human reader. Therefore, the most important characteristic for all practical purposes is not the stand-alone specificity/PPV of the computer, but the combined computer-human diagnostic performance. In this regard, it is important to mention that the majority of false alarms produced by the system were related to calcifications, imaging artifacts, and vessel tracking errors. Those can be easily and rapidly discarded by a human reader, yielding high combined computer-human specificity and PPV. These results are supported by findings in the previous comparison of manual CCTA and automated CCTA.

We should note that the moderate prevalence population had results that are a cause of concern and that should be further discussed. The low-prevalence population has a very low PPV that is counterbalanced by the strong specificity in this population. Also, in the high-prevalence population, the low specificity is counterbalanced by an improved PPV. The moderate prevalence population saw comparative reductions in both specificity and PPV, bringing into question the utility of CAD for CHD in this population. However, considering the previous discussion regarding the nature of the false positive calls, there is still a possibility that CAD might be useful in the moderate prevalence population and, as such, more research must be conducted before eliminating the role of CAD in this population.

Furthermore, with the introduction of the 320-slice CT scanner, we hope for a large improvement in the specificity and positive predictive value of CAD for coronary heart disease, mainly due to its wider volume coverage resulting in significantly less stacking artifact. Improvements in the software, including proper analysis of heavily calcified vessels, as well as improved vessel tracking, can further advance the diagnostic ability of the CAD system.

Conclusions

In this multi-center, retrospective study, we have shown the utility of the CAD for analysis of coronary heart disease using CCTA. By applying the software in 3 distinct clinical sites, we demonstrated that the CAD system is compatible with scans from 3 major CT scanner manufacturers as well as in varying patient populations with different incidences of CHD. In a low-risk population, the CAD system shows as a CAST tool. This is particularly exciting when considering the low prevalence of CHD typically encountered in the emergency department. While both the moderate and high prevalence populations are not viable candidates for the usage of CAD as a CAST tool, the importance in these populations is not lost. First, the inexperienced reader can benefit from a CAD second reader in ruling out false positives the inexperienced reader might encounter. Additionally, an experienced reader can rapidly disregard many of the false positives read by the CAD software leading to an efficient human-computer interface in the diagnosis of CHD using CCTA.

Overall, computer-aided diagnosis in the evaluation of coronary heart disease is starting to become a reality. With this study, we have shown the commercially available CAD system to be a potential candidate to take on this role in various clinical sites with various incidences of coronary heart disease.
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