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Coronary CT Angiography and Assessment of Coronary In-Stent Restenosis—A Brief Report of Stent-Related Factors among Positive Angiographic Cases

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Abstract

Background: In-stent restenosis (ISR) remains a significant concern in coronary artery disease management. This study aims to evaluate the efficacy of coronary computed tomography angiography (CCTA) in detecting ISR and to identify stent-related factors in a real-world patient population.

Methods: This single-center study was conducted over a six-month period in 2024. Patients with a history of PCI who underwent CCTA due to suspected ISR were included, with subsequent invasive coronary angiography (ICA) performed for confirmation. One randomly experienced radiologist evaluated CCTA images for stent characteristics and ISR severity, while two interventional cardiologists assessed ICA results. The association between CCTA findings related to stents and ISR confirmation via ICA was analyzed, and the positive predictive value (PPV) for CCTA in identifying significant ISR was calculated.

Results: A total of 22 patients were included in the study, with a mean age of 62.5 ± 7.3 years. A total of 34 stents were evaluated by CCTA, revealing that 7 stents (20.6%) exhibited ISR with <50% stenosis, while 27 stents (79.4%) had >50% stenosis. The presence of >50% stenosis was statistically significant (p=0.026) associated with ICA findings, with a PPV of 51.8%. Notable variations in PPV were observed based on stent location: proximal left anterior descending artery (LAD) placements had a PPV of 60%, while mid-LAD placements had a PPV of 57.1%. Stents longer than 30 mm demonstrated a higher likelihood of >50% ISR (p=0.011), with a PPV of 76.9%, compared to those measuring 10-20 mm (40%). Additionally, stent diameter was significantly associated with ISR on ICA findings (p=0.024), where larger diameters (>3.5 mm) exhibited an 85.7% PPV for >50% ISR.

Conclusion: Coronary CT angiography serves as an important method for evaluating in-stent restenosis, though its predictive accuracy can differ based on several factors. As a result, is essential to take into account the stent's location within the coronary vessels, as well as its length and diameter. This consideration may assist healthcare professionals in making informed clinical decisions and developing follow-up plans for managing coronary artery disease.

Keywords: In-stent restenosis, Coronary computed tomography angiography, Coronary artery disease, Stent, Positive predictive value, Diagnostic tool

Introduction

Myocardial infarction (MI) and cardiac arrest are among the leading causes of mortality globally, with coronary artery disease (CAD) identified as a primary contributing factor [1]. The advent of percutaneous coronary intervention (PCI), a minimally invasive procedure that involves the implantation of stents to restore blood flow in stenotic coronary arteries, has revolutionized the treatment landscape for CAD [2]. Despite the significant benefits of PCI, including improved survival rates and quality of life for patients, in-stent restenosis (ISR) remains a notable clinical challenge [3]. ISR is characterized by the re-narrowing of a stented coronary artery, and studies indicate that it occurs in approximately 1-2% of patients annually following stent placement [4]. The risk of ISR is influenced by a myriad of factors, including patient demographics (such as age and comorbidities), stent characteristics (type, design, and coating), procedural details (number and location of implanted stents), and the specific vessel involved [3]. To illustrate this, ISR is expected among 20-35% of bare metal stents and 5-10% of drug-covered stents over their lives [5].

Invasive coronary angiography (ICA) is currently regarded as the gold standard for diagnosing ISR [3,5], particularly in patients presenting with acute MI or related symptoms. ICA facilitates direct visualization of the coronary arteries, allowing for accurate assessment of stenosis and enabling further interventions such as repeat PCI or coronary artery bypass grafting (CABG) in cases where significant stenosis (>50%) is identified [6–8]. However, the invasive nature of ICA carries inherent risks, including myocardial injury, vessel dissection, and complications associated with contrast media [4,9]. These risks are particularly pronounced in patients who present with atypical symptoms or non-diagnostic electrocardiogram (ECG) findings. Furthermore, this diagnostic tool might be too expensive, thereby prompting interest in exploring less invasive diagnostic alternatives [9].

Coronary computed tomography angiography (CCTA) has become a promising non-invasive tool for assessing CAD. CCTA offers several advantages, including rapid acquisition of images and the ability to assess coronary anatomy without the need for catheterization. Its diagnostic accuracy for identifying stenoses of 50% or greater, as confirmed by ICA, includes a sensitivity of 85%, specificity of 90%, and a positive predictive value (PPV) of 91% [10]. Moreover, recent studies indicate that CCTA has good sensitivity for identifying ISR, making it a valuable addition to the diagnostic process. Andreini *et al*. reported a sensitivity of 92% and a specificity of 91% for detecting coronary stents with 50% ISR [11]. CCTA provides several benefits, such as quick image acquisition and the ability to evaluate coronary anatomy without catheterization [9]. However, the presence of metallic stents can create artifacts on CCTA images, along with issues like cardiac motion and vessel calcification, which may hinder the accurate evaluation of in-stent restenosis (ISR) [12]. Additionally, interpreting CCTA images for ISR detection requires specialized knowledge that may not always be available in clinical settings [9,11]. These factors can make it difficult to assess, and about 9–10% of stents using CCTA are expected to remain uninterpretable [13]. Despite these challenges, emerging studies suggest that CCTA possesses good sensitivity for detecting ISR, positioning it as a valuable adjunct in the diagnostic workflow. In order to uncover its efficacy, a meta-analysis study evaluating 2,674 patients suspected to have ISR, revealed that CCTA diagnosed 43% of them with ISR and a sensitivity of 90% [14].

This retrospective study aims to evaluate the diagnostic performance of CCTA in detecting ISR within a real-world clinical setting. By comparing CCTA findings with subsequent ICA results, we seek to determine the accuracy of CCTA in identifying ISR and to assess how various stent characteristics—such as location and type—affect CCTA performance. The insights gained from this evaluation will contribute to a better understanding of CCTA's role in the management of patients suspected of ISR and may help refine clinical pathways for diagnosis and treatment in this challenging patient population.

Method

Study design and setting

This retrospective, single-center study was conducted over a six-month period from January to June 2024 at Ghaem Hospital in Mashhad, Iran. The study protocol received approval from the institutional review board, ensuring adherence to ethical standards.

Patient selection

Patients were identified through a comprehensive review of the radiology and cardiology department databases. Inclusion criteria encompassed a history of prior percutaneous coronary intervention (PCI) with stent placement in at least one coronary artery; performance of coronary computed tomography angiography (CCTA) to evaluate for suspected in-stent restenosis (ISR); and subsequent invasive coronary angiography (ICA) performed at Razavi Hospital within three months following the CCTA. Exclusion criteria included: ICA performed at an external institution and insufficient clinical or imaging data for analysis. Each stent placement was analyzed separately to account for patients with multiple stents, allowing for a more granular assessment of ISR.

CCTA acquisition and interpretation

CCTA examinations were conducted using a standardized multi-detector CT scanner (Dual Source SOMATOM Drive - Siemens Healthineers TM), following established protocols for ECG-gated imaging and intravenous contrast administration. Scans were acquired during breath-holding to minimize motion artifacts, with parameters optimized for coronary artery visualization. One randomly experienced radiologist, reviewed and reported the CCTA images.

They assessed each stent based on the following parameters: stent location of coronary artery: categorized as left anterior descending artery (LAD), left circumflex artery (LCX), or right coronary artery (RCA), stent length: measured in millimeters, stent diameter: measured in millimeters, stent placement location: classified as proximal, mid, or distal segment of the coronary artery, degree of ISR : graded as a percentage (%), with specific attention to identifying significant ISR (>50% stenosis). Discrepancies between radiologists were resolved through consensus review.

ICA acquisition and interpretation

ICA procedures were performed according to standard clinical practice guidelines, utilizing a dedicated angiographic system (specify model if known). ICA images were evaluated by two experienced interventional cardiologists who were blinded to the percentage of ISR determined by CCTA but informed of positive CCTA findings indicative of ISR. The degree of ISR was quantitatively assessed using quantitative coronary angiography (QCA), with ISR defined as >50% diameter stenosis. The interventional cardiologists documented their findings on stent patency and any additional lesions that may require intervention.

Data analysis

Data obtained from CCTA and ICA were entered into SPSS software version 11.5 for statistical analysis. Descriptive statistics were calculated for patient demographics and stent characteristics. Frequency distributions for stent location, length, diameter, placement location, and degree of ISR were presented in tabular format. Patients were categorized into two groups based on ICA findings: those with >50% ISR and those with ≤50% ISR [7,8]. PPV was evaluated among the patients for patients with >50% ISR in CCTA, and confirming with >50% ISR on ICA. Furthermore, the association between CCTA findings and ISR severity was evaluated using the Chi-square and Fischer test. A significance level was set at $p<0.05$.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and received approval from the Ethics Committee of Mashhad University of Medical Sciences. Informed consent was obtained from all patients regarding the retrospective nature of the study, ensuring that patient identities and personal information remained confidential throughout the research process. All data were anonymized prior to analysis to protect patient privacy.

Results

In order to describe the process of data collection, 38 patients had been reported with a diagnosis of ISR by CCTA findings. However, 16 patients were not referred for ICA, subsequently, 22 patients were entered into the study. There was a dominancy of the male gender (14 vs 8) and a mean age of 62.5±7.3 years old. Thirty-four stents were reported to have some degree of ISR after CCTA evaluation of all stents of these patients, and the following report is about the 34 stents.

As can be seen from **Table 1**, 7 (20.6%) had an ISR with <50% stenosis, while 27 (79.4%) had >50% stenosis. Regarding these stents, the presence of >50% stenosis was statistically significant (p=0.026), yielding a PPV of 51.8%, calculated as the proportion of stents confirmed to have >50% stenosis via ICA compared to those identified with >50% stenosis by

Table 1. CCTA finding and its association with ICA report, and PPV.

Variables		Frequency (%)	Number of ICA with <50% ISR	Number of ICA with >50% ISR	P value	Stents which ICA confirmed >50% ISR /CCTA showed with >50% ISR=PPV (%)
CCTA ISR	<50% stenosis	7 (20.6)	7	0	**0.026**	14/27=51.8
	>50% stenosis	27 (79.4)	13	14		
Stent Location	LAD	16 (47.1)	9	7	0.54	7/12=58.3
	LCX	8 (23.5)	6	2		2/6=33.3
	RCA	10 (29.4)	5	5		5/9=55.6
Stent Placement Location	Proximal	15 (44.1)	10	5	0.774	5/11=45.4
	Mid	12 (35.3)	6	6		6/10=60
	Distal	7 (20.6)	4	3		3/6=50
Stent Length	10–20	15 (44.1)	11	4	**0.011**	4/10=40
	20–30	5 (14.7)	5	0		0
	More than 30	14 (41.2)	4	10		10/13=76.9
Stent Diameter	2.5–3	12 (35.3)	9	3	**0.024**	3/9=33.3
	3–3.5	15 (44.1)	10	5		5/11=45.4
	More than 3.5	7 (20.6)	1	6		6/7=85.7
Total		34 (100)	20	14		14/27=51.8

CCTA: Computed Tomography Angiography; ICA: Invasive Coronary Angiography; ISR: In-Stent Restenosis; LAD: Left Anterior Descending Artery; LCX: Left Circumflex Artery; PPV: Positive Predictive Value; RCA: Right Coronary Artery

CCTA. While there was no significant association between stent location and the presence of >50% ISR (p=0.54), the PPV varied across locations: LAD (58.3%), LCX (33.3%), and RCA (55.6%). Similarly, the stent placement location (proximal, mid, distal) did not significantly correlate with ISR (p=0.774), but PPV was higher in the mid-section.

While the overall stent location was not significantly associated with the presence of >50% ISR (p=0.54), notable variations in PPV were observed depending on the specific location within the coronary vasculature (not mentioned in table). Specifically, proximal LAD placements yielded a PPV of 60%, and mid-LAD placements had a PPV of 57.1%. In contrast, stents placed in the obtuse marginal (OM) branch of the LCX and the proximal RCA demonstrated a PPV of 100%. Conversely, CCTA exhibited a PPV of 0% for ISR >50% stenosis in the proximal LCX.

Moreover, **Table 1** reveals that a statistically significant association was found between stent length and the degree of ISR (p=0.011). Specifically, patients with stents longer than 30 mm were more likely to have >50% ISR compared to patients with stents between 10-20 mm. The PPV for stents >30 mm was 76.9%, whereas it was only 40% for stents between 10-20 mm. Furthermore, stent diameter was significantly associated with the degree of ISR (p=0.024). Larger stent diameters (>3.5 mm) showed a higher PPV for detecting >50% ISR (85.7%) compared to smaller stent diameters (2.5-3 mm: 33.3%; 3-3.5 mm: 45.4%).

Discussion

In the present investigation, one of the key findings is the notably high incidence of in-stent restenosis (ISR) exceeding 50%, as identified through coronary computed tomography angiography (CCTA) at a rate of 79.4%. This statistic highlights the persistent clinical challenge posed by ISR, despite ongoing improvements in stent design and advancements in antiplatelet therapy. This association supports the efficacy of CCTA in detecting clinically significant ISR. However, the positive predictive value (PPV) of 51.8% indicates that while CCTA is a useful diagnostic tool, it may also lead to an overestimation of ISR severity compared to similar prior studies [6,12,14,15]. The possible reason behind this discrepancy and difference with previous research might be the varying levels of expertise among radiologists, the quality of CT imaging, or the imaging protocols employed in our country. Although the positive likelihood ratio was not assessed in the current study, previous research by Dahdal, which reviewed 20 studies, reported a rate of 7.17 among patients with ISR [14].

The variability in PPV across different coronary artery locations is particularly striking. While there was no significant association between overall stent location and ISR greater than 50% (p=0.54), the PPV exhibited considerable variation depending on the specific artery involved. The LCX demonstrated the lowest PPV at 33%. In a similar study, the left main coronary artery (LMCA) showed a remarkable PPV of 100% after evaluating 184 stents via CCTA, while other arteries such as the LCX, RCA, and LAD displayed PPVs ranging from 50% to 60% [11]. Although no patients with LMCA stents were identified in our study, the high PPV might be attributed to the larger lumen diameter associated with these stents. Additionally, proximal LAD placements yielded a PPV of 60%, Nakamura *et al*., have indicated higher diagnostic accuracy for stents located in this region (proximal LAD) in comparison with other regions [15]. This variation in PPV likely reflects differences in anatomical characteristics, plaque load, and hemodynamic factors across various coronary segments. Our findings suggest that CCTA may be particularly reliable in assessing ISR in specific locations like the obtuse marginal (OM) and proximal RCA, while caution is warranted in interpreting results for some regions.

The statistically significant associations observed between stent length and diameter with the higher PPV of ISR (p=0.011 and p=0.024, respectively) are among the most compelling findings of this brief report. The observation that longer stents (>30 mm) were more likely to exhibit ISR exceeding 50%, as well as the higher PPV for detecting such ISR (76.9% vs. 40% for 10–20 mm), suggests that CCTA might be more reliable in identifying significant restenosis in patients with longer stents. The fact that we found this association with a statistically significant value is a confirmation of previous research demonstrating a strong correlation between stent dimensions and the subsequent risk of restenosis. However, the potential presence of more artifacts with longer stents should also be considered, which could potentially lead to an overestimation of the severity of stenosis.

The association between larger stent diameters and higher PPV for detecting >50% ISR (85.7% for >3.5 mm vs. 33.3% for 2.5-3 mm and 45.4% for 3–3.5 mm) also merits careful consideration. This finding is supported by Wang *et al*., who noted that dual-source CT identified a greater number of ISR cases in stents with inner diameters below 3.0 mm [16]. Additionally, these findings are confirmed in a systematic review performed by Pugliese *et al*., suggesting false positive findings in stents with a diameter less than 2.75 mm [17]. Surprisingly, they found that other stent-related factors (except for stent inner diameter) have not had any significant impact on the accuracy of CCTA report about ISR. It is important to note that thinner stents (100 micrometers) were found to reduce artifacts significantly and might have a positive impact on the accuracy of CCTA in the detection of ISR, although this variable was not assessed within our study [18].

Limitations

Several limitations of this study warrant consideration. First, the sample size (n=22 patients, 34 stents) is relatively small, limiting the statistical power and generalizability of the findings. Second, the retrospective nature of the study introduces the potential for selection bias. The fact that 16 patients with CCTA-diagnosed ISR did not undergo ICA raises questions about the reasons for this discrepancy and its potential impact on the study results. Third, the study relies on ICA for assessing ISR, which has inherent limitations. ICA, while considered the gold standard, is invasive and carries its risks. Furthermore, ICA provides a two-dimensional angiographic view, which may not accurately reflect the three-dimensional morphology of ISR. Fourth, the study does not account for other potential risk factors for ISR, such as diabetes mellitus, smoking, hyperlipidemia, and the type of stent used (e.g., drug-eluting vs. bare-metal stents). These factors could confound the relationship between stent-related factors and ISR.

Conclusion

This brief report provides valuable insights into the role of coronary CT angiography in the assessment of in-stent restenosis and the influence of stent-related factors on the development of in-stent restenosis. While coronary CT angiography offers a non-invasive means of detecting in-stent restenosis, its limitations, particularly the potential for overestimation of stenosis severity in certain coronary locations, must be considered. The observed variability in positive predictive value across different coronary segments underscores the importance of considering the anatomical context when interpreting coronary CT angiography results. Further research is needed to refine the use of coronary CT angiography in this clinical setting and to develop strategies to minimize the risk of in-stent restenosis. Further investigation is warranted to determine the reasons for the variability in positive predictive value across different coronary locations and to develop strategies to mitigate these differences. Additionally, research is needed to evaluate the impact of different stent types and antiplatelet regimens on the risk of in-stent restenosis about stent-related factors. Finally, exploring the cost-effectiveness of coronary CT angiography compared to other diagnostic modalities in the evaluation of in-stent restenosis would be valuable.

Declarations

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Data availability

The datasets utilized and analyzed during this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The study was overseen by the ethics committee of Mashhad University of Medical Sciences. Informed consent was obtained from all participants. Before each interview, participants received comprehensive information about the study's objectives, and written consent was secured. They were also informed of their right to withdraw from the study at any time.

Consent for publication

Not applicable.

Competing interests

The authors declare that there are no competing interests.

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