

# Correlations Between the Contrast Density Gradient along the Coronary Stents and Functional Significance of In-stent Restenosis

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## ABSTRACT

**Introduction:** Coronary artery disease (CAD) is the leading cause of death worldwide and is associated with a significant socio-economic impact. In many cases, patients are treated with implanted coronary stents that carry a significant risk for reobstruction. The **aim** of our study was to evaluate the importance of coronary computed tomography angiography (CCTA) in evaluating the significance of in-stent restenosis lesions and for establishing the indication for reintervention in these cases. **Materials and methods:** We evaluated 25 patients who underwent CCTA examination. We determined the contrast density, expressed in Hounsfield units at two levels, proximal and distal to the stent. **Results:** There were no statistically significant differences between the study groups in terms of gender (41.17% females in Group 1 vs. 37.5% in Group 2,  $p = 1$ ), presence of hypertension (41.17% in Group 1 vs. 62.5% in Group 2,  $p = 0.31$ ), smoking status (41.17% in Group 1 vs. 37.5% in Group 2,  $p = 0.31$ ), incidence of dyslipidemia (47.05% vs. 50%,  $p = 1$ ) and diabetes mellitus (35.29% vs. 0%,  $p = 0.31$ ). However, the age of the study population was significantly higher in the groups with significant ISR ( $58.94 \pm 8.35$  vs.  $47.25 \pm 11.2$ ,  $p = 0.02$ ). Patients who showed significant angiographic in-stent stenosis (more than 70%) were found to have a higher transluminal attenuation gradient, compared with those with less severe lesions ( $14.5 \pm 5.4$  vs.  $5.14 \pm 2.4$ ,  $p = 0.02$ ). **Conclusions:** The transluminal attenuation gradient, assessed by CCTA is a non-invasive-derived parameter that can help the clinician to determine the right time for revascularization in case of in-stent restenosis.

**Keywords:** in-stent restenosis, CT coronary angiography, transluminal attenuation gradient

## INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death worldwide and is associated with a significant socio-economic impact. In many cases, patients are treated with implanted coronary stents that carry a significant risk for reobstruction.

Nowadays, the identification and treatment of in-stent restenosis represents one of the cardiologists' main challenges. Coronary revascularization with stents led to the development of a new pathology represented by in-stent restenosis (ISR). The development of new antiplatelet drugs represented important steps for the prevention of ISR, and the incidence of in-stent restenosis has been partially reduced by the appearance of new types of medication releasing stents.<sup>1</sup>

Currently, the trend in the treatment of cardiologic pathologies is to pass from invasive procedures to non-invasive or minimum-invasive. Therefore, coronary revascularization tends to pass from surgical to interventional methods, which are less invasive. This is due to both a smaller surgical risk and the fact that the patient accepts more easily a wrist puncture than a thoracic intervention that requires induced cardiac arrest and its afferent risks. By these means, the diagnostic methods tend also to become more non-invasive, this is why Multislice Computed Tomography tends to replace the classical invasive coronary angiography for the diagnosis of ISR.<sup>2,3</sup>

## STUDY AIM

The aim of our study was to evaluate the importance of Coronary Computed Tomography Angiography (CCTA) in evaluating the significance of in-stent restenosis lesions and for establishing the indication for re-intervention in these cases.

## MATERIALS AND METHODS

We included 25 patients with in-stent restenosis that underwent CCTA. All examinations were performed using multi slice 64 Somatom Sensation CT (Siemens, Germany), that includes a special software for CT angiography, allowing coronary evaluation (Figure 1). We excluded patients with

renal impairment, allergy to iodine and diabetes patients with oral treatment. Most of the patients were under re-evaluation at 1 year after stent implantation (our protocol) or underwent prior stent implantation and had stable angina/non-specific chest pain. The CT Angiography protocol consisted in the following: after laboratory tests and after the patient has signed the informed consent, we evaluated the patient's heart rate and kept it to a level under 60 beats per minute (by administering Metoprolol); an intravenous line was placed for contrast administration in the right ante-cubital vein through which a contrast agent was administered with a rate of 1 ml/kg, followed by saline perfusion (150 ml). The angiographic evaluation was performed with a specialized software and the reconstructions were analyzed by a radiology specialist. We determined the contrast density expressed in Hounsfield units (HU) at two levels, proximal and distal to the stent (Figure 2). The contrast density gradient was easily calculated by the cursor placement, the software showing the contrast density gradient. Clinical and laboratory data were also noted.

The statistical analysis was performed using Microsoft Excel 2007 and MedCalc 16.4.3 statistical software.

The patients were divided into 2 groups according to the cut-off value of 70% degree of in-stent restenosis: Group 1: 17 patients (68%) with  $\geq 70\%$  restenosis; Group 2: 8 patients (32%), with  $< 70\%$  in-stent restenosis.

The study has been carried out in accordance with the code of ethics of the World Medical Association's Declaration of Helsinki. All patients gave written informed consent, and the study protocol was approved by the ethics committee of the Cardio Med Medical Center, the center where the study was conducted.

## RESULTS

There were no statistically significant differences between the study groups in terms of gender (41.17% females in

**TABLE 1.** Patient baseline characteristics

Patient baseline characteristics	Group 1 $\geq 70\%$ restenosis	Group 2 $< 70\%$ restenosis	p value
Age	58.94 $\pm$ 8.35	47.25 $\pm$ 11.2	0.02
Female gender	7 (41.17%)	3 (37.5%)	1.00
Male gender	10 (58.82%)	5 (62.5%)	
Arterial Hypertension	7 (41.17%)	5 (62.5%)	0.31
Smoking	7 (41.17%)	3 (37.5%)	0.31
Dyslipidemia	8 (47.05%)	4 (50%)	1.00
Diabetes Melitus	6 (35.29%)	0 (0%)	0.31
Total	17 (68%)	8 (32%)	



**FIGURE 1.** Angio CT reconstruction of a coronary stent implanted in the left anterior descendant artery

Group 1 vs. 37.5% in group 2,  $p = 1$ ), presence of hypertension (41.17% in group 1 vs. 62.5% in Group 2,  $p = 0.31$ ), smoking status (41.17% in Group 1 vs. 37.5% in Group 2,  $p = 0.31$ ), incidence of dyslipidemia (47.05% vs. 50%,  $p = 1$ ) and diabetes mellitus (35.29% vs. 0%,  $p = 0.31$ ). However, the age of the study population was significantly higher in the groups with significant ISR ( $58.94 \pm 8.35$  years vs.  $47.25 \pm 11.2$  years,  $p = 0.02$ ).

From the total of 25 patients, 70% underwent primary PCI for acute myocardial infarction. There were no statistically significant differences between the 2 groups in terms of cardiovascular risk factors, but we observed that pa-



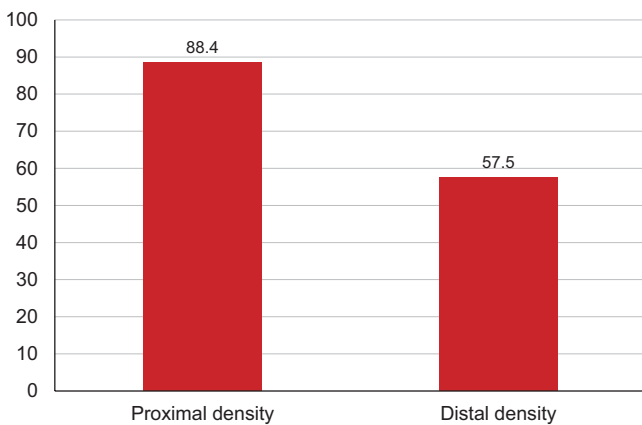
**FIGURE 2.** Measurement of contrast density at two levels: proximal and distal to the stent

tients with an ISR higher than 70% were significantly older compared to the other group (Table 1).

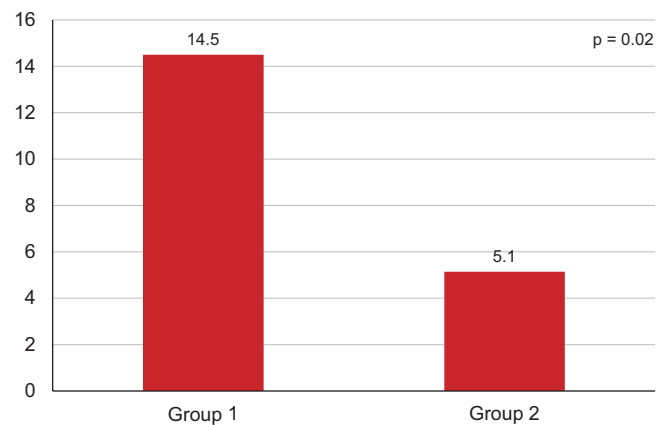
The average dye density was 88.4 HU (proximally) and 57.5 HU distally (Figure 3). We found a good correlation between the contrast attenuation gradient and the degree of in-stent narrowing. In case of patients that had  $\geq 70\%$  in-stent restenosis, the transluminal attenuation gradient was significantly higher as compared to those with  $< 70\%$  in-stent restenosis ( $5.14 \pm 2.7$ , vs.  $14.5 \pm 5.4$ ,  $p = 0.02$ ) (Figure 4).

## DISCUSSIONS

The functional significance of a coronary artery stenosis or of an in-stent restenosis is important in order to establish the indication for interventional treatment in these cases. It is well-



**FIGURE 3.** The average contrast density proximal and distal to the stent



**FIGURE 4.** The transluminal contrast gradient attenuation in the study groups

known that a revascularisation procedure is indicated in case of a symptomatic coronary stenosis with a more than 70% lumen reduction, however there are not enough studies to indicate the ideal moment for a reintervention in case of ISR.

Given the great number of patients treated with stent coronary angioplasty, the cardiologist is faced with a great number of cases in which the patient wants to know about the stent evolution.<sup>4</sup>

Computed tomography coronary angiography is a non-invasive diagnostic tool that can be useful in the daily practice,<sup>5</sup> helping the clinician to follow the evolution of the atherosclerotic plaque, as well as the evolution of the remaining lesions in patients with previously implanted coronary stents.<sup>6</sup> CCTA assessment of the transluminal contrast gradient throughout the stent is a valuable method in diagnosing the degree of in-stent intimal hyperplasia, and it could be a useful method for the indication of the optimal time for re-intervention in case of significant in-stent restenotic lesions.

## CONCLUSIONS

The contrast density gradient along the stent, measured by CCTA, significantly correlates with the severity of ISR and can represent a useful marker for the assessment of the functional significance of ISR via a non-invasive route. The transluminal attenuation gradient, assessed by CCTA is a non-invasive-derived parameter that can help the clinician to determine the right time for the revascularization in case of in-stent restenosis.

## CONFLICT OF INTEREST

Nothing to declare.

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