

Role of Multidetector Computerized Tomography in Coronary In-Stent Restenosis

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ABSTRACT

We described the role of multi detector computerized tomography in the detection and exclusion of coronary in-stent re-stenosis compared with the conventional coronary angiography.

PATIENTS AND METHODS: 30 patients pretreated with coronary stenting and complaining of angina like symptoms underwent dual source coronary angiography one day before performing conventional coronary angiography.

RESULTS: 47 stents were examined 43 of them were assessable by DSCT-CA and the calculated sensitivity, specificity, negative predictive value, positive predictive value and overall accuracy of all assessable stents were 100%, 90%, 100%, 81% and 93%, respectively. When analyzing the results for stents ≤ 2.75 mm in diameters the results were less encouraging, The calculated sensitivity, specificity, negative predictive value, positive predictive value and overall accuracy of all assessable stents were 100%, 70%, 100%, 40% and 75%, respectively.

CONCLUSION: With the high sensitivity and negative predictive value -reaching up to 100%- with dual source CT scanners, it could be used confidently to rule out in-stent re-stenosis. However, due to the frequent false positive results, careful patient selection should be done.

Key words: Multidetector Computerized Tomography, Coronary In-Stent Restenosis

Introduction

Stent implantation in human coronary arteries, initiated in 1986 by Sigwart *et al.* is intended to reduce coronary restenosis (**Hoffmann and Mintz 2000**). The long term outcome of stent implantation is affected by a process called in stent restenosis (ISR) (**Mitra and Agrawal 2006**). Compared with balloon angioplasty alone, where the chance of restenosis is 40%, stents reduce the chance

of restenosis to 25% (**Dangas and Kuepper 2002**). As a result, in-stent restenosis has developed into a significant clinical problem (**Hoffmann and Mintz 2000**). In-stent restenosis is typically seen 3 to 6 months after the procedure (**Dangas and Kuepper 2002**).

A noninvasive detection of ISR would be of clinical importance in the treatment and follow-up of coronary artery

disease. The CTCA is less invasive and less expensive than ICA, which reduces physical, mental, and economical stress, as well as potential complications, especially for patients who require repeat coronary angiography (**Ehara et al 2007**). Despite substantial technologic progress, stent imaging continues to be a challenge for CT, mainly because stent-related artifacts result in higher CT attenuation values and artificial narrowing of the lumen (**Oncel et al 2008**).

Dual-source CT provides significantly better diagnostic image quality than single-source CT despite higher heart rates in the dual-source CT group (**Donnino et al 2009**). The high temporal resolution of dual-source CT may help to reduce artifacts caused by severe calcifications, also dual-source CT performed well in determination of the presence of stent occlusion and in-stent restenosis (**Oncel et al, 2008**).

Stent size and material can affect evaluability by CCTA (**Rixe et al 2006**, **Lin et al 2009**). Although DSCT-CA leads to frequent false positive findings in smaller stents (≤ 2.75 mm), it reliably rules out in-stent restenosis irrespective of stent size (**Pugliese et al 2008**). Magnesium is the most favorable stent material for imaging. Stainless-steel and cobalt stents are also favorable. Other factors that can potentially limit stent evaluability include overlapping positioning, strut thickness, and large patient size (**Lin et al 2009**). Thus, MDCT may be appropriate for

stent assessment in only selected patients (**Wykrzykowska et al 2010**).

Patients and methods

In this study 30 patients all of them were men with mean age 65 years; range (44–79 years) with 47 stents were examined between August 2010 and January 2012; all the stents were made of cobalt and stainless steel both drug eluting and non-drug eluting. All patients were scheduled to undergo invasive coronary angiography for in-stent restenosis suspected on the basis of the patient's reports of symptoms. Dual-source CT examinations were performed 1 day before catheterization.

Exclusion criteria for dual-source CT were allergy to contrast medium, renal insufficiency (serum creatinine concentration > 1.5 mg/dL) not on regular dialysis, unstable clinical condition, and inability to perform a breath-hold. All other patients with previously implanted stents were eligible for the study.

Patient Preparation:

All the patients were admitted to hospital, underwent serum creatinine analysis, and were fasting for 6 hours before the examination. Sublingual nitrate was given 5 minutes before image acquisition to dilate the coronary arteries.

Scan Protocol:

All CT examinations were performed on a 128 dual-source CT scanner (Siemens Somatom Definition

Flash). The coronary angiographic scan was obtained with injection 70 mL of nonionic contrast medium (370 mg I/mL iopromide, ultravist) at a flow rate of 6 mL/s followed by 50 mL of saline solution (injection rate 5 mL/s) to wash out the contrast material from the right ventricle.. Contrast administration was controlled with test bolus. The scan parameters were collimation: 128 x 0.6 mm, spatial resolution: 0.33 mm, temporal resolution: 75 ms, scan time: 4 s, scan length: 96 mm, rotation time: 280 ms, 120 kV, 265 mAs/rotation, effective dose: 3.6 mSv, pitch 0.2-0.47 adapted to the heart rate.

Image Reconstruction:

Retrospective gating technique was used to synchronize data reconstruction with the ECG signal. The reconstructions were made in diastole at a slice thickness of 0.6 mm and a reconstruction increment of 0.5 mm. The reconstruction interval with the fewest motion artifacts was chosen and used for further analysis. To decrease stent-related artifacts, edge-enhancing high-spatial-resolution kernels (B46f) were used for reconstruction.

Noninvasive MDCT Angiographic Analysis:

Analysis of scans was performed at a workstation (Wizard, Siemens Medical Solutions) equipped with dedicated cardiac post-processing software (Syngo Circulation, Siemens Medical Solutions). Data sets were evaluated on both the original axial images and

multiplanar reformatted reconstructions orthogonal and perpendicular to the vessel course. Curved multiplanar reformations were made both manually and with automated software. Contrast enhancement within the lumen of the stented segment was compared visually with enhancement in the unstented portion of the artery. Short-axis views were examined at various points along the stent, particularly where reduced luminal enhancement was identified.

The assessability of each stent was determined. A stent was considered assessable when the stent lumen was visible and contrast attenuation of the lumen could be evaluated qualitatively without the influence of partial volume effects, metal artifacts of stents, or cardiac motion artifacts.

Stents were visually evaluated and defined as Patent with no visible neointimal hyperplasia (absence of low-attenuation areas related to neointimal tissue), Patent with nonocclusive neointimal hyperplasia (longitudinal low-attenuation areas along the stent wall observed as a rim of hypoattenuation between the stent and the contrast enhanced vessel lumen with residual lumen > 50%), Patent with in-stent restenosis (longitudinal and transverse low-attenuation areas along the stent wall with residual lumen \leq 50%), or In-stent occlusion (complete loss of attenuation inside the stent lumen). The presence of

re-stenosis was defined as 50% or greater narrowing of the luminal diameter.

Invasive Coronary Angiography:

Invasive coronary angiography was performed on all patients with standard techniques 1 day after the CT examination. The angiograms were evaluated by one experienced cardiologist blinded to the results of dual-source CT angiography. Restenosis was defined as 50% or greater stenosis anywhere within the stent. As in the CT evaluation, stents were defined as patent with no intimal hyperplasia, patent with neointimal hyperplasia (residual lumen > 50%), patent with in-stent restenosis (residual lumen ≤ 50%), or occluded.

Statistical Analysis:

Table 1 showing the results of DSCT CA and conventional angiography. No statistical difference notice as the $p > 0.05$.

		Angio- graphy	CT	Chi- Square	P- value
Restenosis	N	13	16	0.468	0.49 4
	%	30.2	37.2		
patent	N	30	27		
	%	69.8	62.8		
Total	N	43	43		
	%	100.0	100.0		
			0		

Statistical analysis was performed with SPSS 12.0 (SPSS) for Microsoft Windows. The diagnostic performance of dual-source CT angiography in evaluation of coronary stent restenosis and occlusion was determined with respect to the results

of per-stent analyses. Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated. The chi-square test used to determine whether there was a statistically significant difference between dual-source CT angiography and invasive coronary angiography in the evaluation of coronary stents. A value of $p < 0.05$ was considered statistically significant.

Only the evaluable stent images were included in the statistical analysis.

Results

A total of 47 stent in 30 patients were examined only 43 (91%) stents were evaluable by dual source CT. All the inevaluable stents were ≤2.5mm in diameter. 16/43 stents were diagnosed by CT as re-stenosed and 27/43 stents were diagnosed as patent; while by conventional angiography 13/43 stents were diagnosed as re-stenosed and 30 stents were diagnosed as patent with no significant statistical difference between the two modalities as the chi square test shows $p = 0.494$ (*table 1*).

Only 3/16 stents were falsely diagnosed as significantly re-stenosed and were all ≤2.75mm in diameter. The calculated sensitivity, specificity, negative predictive value, positive predictive value and overall accuracy of all assessable stents were 100%, 90%, 100%, 81% and 93%, respectively. Regarding stents ≤2.75mm, the results were less encouraging. 5/12 stents were diagnosed by DSCT CA as re-stenosed, 7/12

diagnosed patent; while the conventional angiography showed 2/12 stents re-stenosed, and 10/12 stents patent. High percentage of false positive diagnosis of stent re-stenosis 3/5 was observed, which is statistically significant as the chi square test shows p 0.018, (*table 2*).

Table 2 showing the false and positive results of DSCT CA regarding stents ≤ 2.75 mm in diameter with $p < 0.05$ indicating significant statistical difference.

		re-stenosis	Chi-Square	P-value
true +ve	N	2	5.600	0.018
	%	40.0		
false +ve	N	3		
	%	60.0		
Total	N	5		
	%	100.0		

The calculated sensitivity, specificity, negative predictive value, positive predictive value and overall accuracy of assessable stents ≤ 2.75 mm were 100%, 70%, 100%, 40% and 75%, respectively.

Discussion

Although there is no available research on 128 DSCT, yet we compared our results with researches on 64 DSCT which has the closest physical properties to our device. In our study using 128 DSCT we found 91% of stents are assessable; all of the inevaluable stents were < 2.75 mm, while **Pugliese et al (2008)** using 64 DSCT reported that 95% of stents assessable and all the non-

assessable stents were < 2.75 mm in diameter which is similar to our results, while **Oncel et al (2008)** using 64 DSCT found all stents are assessable and they attributed this to the fact that most examined stents were larger than 3mm in diameter while in our study 25% of evaluated stents were ≤ 2.75 mm in diameter.

We found sensitivity, specificity, negative predictive value, positive predictive value and overall accuracy of all assessable stents were 100%, 90%, 100%, 81% and 93%, respectively; these results are in close proximity to the results of **Oncel et al (2008)**, however slightly different from the results of **Pugliese et al (2008)** as they reported sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 94%, 92%, 77% and 98%, respectively and this could be attributed to the difference in number of evaluated stents, 43 in our study and 178 in **Pugliese et al (2008)** study or to the difference in the scanners used; in our study 128 DSCT with temporal resolution 75ms in comparison to 64 DSCT with 85ms temporal resolution as the higher temporal resolution may help to reduce artifacts and better visualization of stent lumen (**Oncel et al 2008**). There was close similarity between our study and **Pugliese et al (2008)** study regarding their evaluation of stents ≥ 3 mm; they reported sensitivity and NPV 100%, specificity 97% and PPV 91%; while their results were lower

when considering stents ≤ 2.75 mm in diameter to be sensitivity 84%, specificity 64%, PPV 52%, NPV 90% which affected the overall results when considering stents of all sizes.

No difference was found between drug eluting and non-drug eluting stents which are similar to the fore-mentioned two studies. Also all examined stents were made of stainless steel and cobalt, two materials reported to be favorable with CT evaluation (**Oncel et al 2008**, **Mahnken et al 2004** and **Scheffel et al 2006**), so the material of the stents had no influence on the assessability of the in-stent lumen.

Stent size had the greatest effect, where the specificity, positive predictive value and accuracy of stents ≤ 2.75 mm in diameter dropped to 70%, 40% and 75%, respectively, due to the frequent false positive results which is comparable to the results of **Pugliese et al (2008)**. According to **Dewey et al (2011)** the frequent false positive results are attributed to the blooming artifact which leads to artificial stent lumen narrowing. The in-stent lumen is systematically underestimated in CT; artificial narrowing ranges from 20% to 100% depending on stent material. When using current state of the art MDCT with smaller slice thickness and dedicated reconstruction kernels, artificial narrowing is reduced but still considerable at about 30–40%.

Conclusion

The higher the spatial resolution of the scanner the better the visualization

of the in-stent lumen until a certain level where the spatial resolution of all scanners is same i.e. 64 slice and more MDCT scanners, then the difference will be generated from the temporal resolution of the scanner, with the higher the temporal resolution the better the image quality and in-stent visibility.

Stent size has the main determining factor of the usefulness of the CT usage in evaluating the stent lumen. In modern devices 2.75mm is the cutoff above it the accuracy is highest.

With the high sensitivity and negative predictive value -reaching up to 100%- with dual source CT scanners, it could be used confidently to rule out in-stent re-stenosis. However, due to the frequent false positive results, careful patient selection should be done, i.e. the stent diameter should be > 2.75 mm, the stent material should be favorable with CT e.g. stainless steel, magnesium or cobalt. Also MDCT shouldn't be used for routine evaluation of stent patency and reserved for those who are candidate for invasive coronary angiography, as the frequent false positive results may expose unnecessary patients to invasive technique.

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دور التصوير المقطعي بالحاسب في عودة الضيق الأوعية التاجية داخل الدعامات

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الملخص

قمنا بوصف دور التصوير المقطعي المحوسب للكشف عن دوره في الكشف واستبعاد الضيق في دعامات الشريان التاجي بالمقارنة مع تصوير الأوعية التاجية والتقليدية.

المرضى والطرق :

خضع 30 مريضاً سبق تجهيزهم بالدعامات التاجية كانوا يشكون من أعراض الذبحة الصدرية وأعراض تشبه أعراض مصدر مزدوج تصوير الأوعية التاجية يوم واحد قبل تنفيذ تصوير الأوعية التاجية التقليدية. وكان 43 من إجمالي 47 تم فحصهم لتقييم الدعامات، من قبل بالتصوير المقطعي – يعانون من الحساسية ، والنوعية، القيمة التنبؤية السلبية، القيمة التنبؤية الإيجابية ودقة الشاملة لجميع الدعامات للتقييم ونسبة 100%، 90%، 100%، 81% ، 93% على التوالي.

النتيجة :

عند تحليل نتائج الدعامات ≥ 2.75 مم بأقطار كانت النتائج مشجعة أقل، حساسية حساب، والنوعية، القيمة التنبؤية السلبية، القيمة التنبؤية الإيجابية ودقة الشاملة لجميع الدعامات للتقييم ونسبة 100%، 70%، 100%، 40% و 75%، على التوالي.