Multi-detector row CT angiography in the assessment of coronary in-stent restenosis: A systematic review

Abstract

Purpose: The aim of this study was to perform a systematic review of the diagnostic accuracy of multi-detector row computed tomography angiography (MDCT) for detection of coronary in-stent restenosis in patients treated with coronary stenting when compared to invasive catheter angiography.

Materials and Methods: A search of PUBMED and MEDLINE databases for English literature was performed. Only studies with at least 10 patients comparing 16- or more detector rows MDCT angiography with invasive catheter angiography in the detection of coronary in-stent restenosis (more than 50% stenosis) were included for analysis. Sensitivity and specificity estimates pooled across studies were tested using a fixed effects model.

Results: 15 studies met selection criteria for inclusion in the analysis. There were eight studies performed with 16-detector row CT scanners, and five studies with 64-detector row scanners and one study with a 40-detector scanner. The remaining study was performed with a mixture of 16-and 64-detector row scanners. Prevalence of in-stent restenosis following coronary stenting was 18% (95% CI: 13%, 24%). Pooled estimates of the sensitivity and specificity of overall MDCT angiography for the detection of coronary in-stent restenosis was 85% (95% CI: 78%, 90%) and 97% (95% CI: 95%, 98%), respectively. No significant difference was found between 16- and 64-detector row scanners regarding the sensitivity and specificity of MDCT for assessment of in-stent restenosis ($p>0.05$).

Conclusion: The results showed that MDCT angiography (with 16 or more detector rows) has moderate sensitivity and high specificity for the detection of coronary in-stent restenosis when compared to invasive catheter angiography. A high specificity value of MDCT may be most valuable as a non-invasive technique of excluding coronary stent restenosis or occlusion. The main factors affecting visualization are stent diameters and stent materials.

Key words: Multi-detector computed tomography, stent, restenosis, coronary artery disease, artifacts

Introduction

In recent years, coronary artery disease has been increasingly treated by coronary stent placement. Although stent implantation has been shown to greatly reduce restenosis after balloon angioplasty (1, 2), in-stent restenosis can occur in 20-35% of patients for bare metal stents (3, 4), and 5-10% for drug-eluting stents (3, 4), as demonstrated by intravascular ultrasound. Invasive coronary angiography remains the gold standard technique for detection of in-stent restenosis. However, coronary angiography has limitations due to its invasiveness and association with potential risks of morbidity and mortality. Given the high number of patients who receive coronary stents yearly, a non-invasive imaging technique for detection of in-stent restenosis will be clinically important and beneficial.

Multi-detector row computed tomography (MDCT) is increasingly used for non-invasive imaging of coronary artery disease and has been reported to have a high diagnostic accuracy in the detection of coronary artery stenosis, especially when the latest fast 64-detector row scanners are used (5, 6). However, imaging of coronary stents by MDCT is more difficult than native coronary artery. This is due to the presence of the metal within the stents that can cause artifacts interfering with the interpretation of lumen patency. Although several reports have shown that MDCT may be used to evaluate stent patency, more precise evaluation of the lumen within the stent is markedly affected by the blooming artifacts that can cause an appearance of artificial enlargement of the metallic stent struts (7-10). Results of both in vitro and vivo studies have shown that reliable direct assessment of the stent lumen with 4-detector row CT is not possible (7, 8). With increasing number of detector rows, promising results of MDCT in coronary artery disease have been reported with improved spatial and temporal resolution (11-13). However, it is unclear whether this also applies to the assessment of coronary stent implantation. Thus, the aim of this study was to perform a meta-analysis, based on the currently available published results, of the diagnostic accuracy of 16-or more detector rows MDCT angiography for the detection of coronary in-stent restenosis compared to invasive catheter angiography.

Materials and Methods

Criteria for data selection and literature screening

A search of PUBMED and MEDLINE databases for English literature was performed by two reviewers for articles describing the diagnostic value of MDCT angiography in coronary artery stenting when compared to conventional invasive catheter angiography. Inclusion criteria required that articles must be peer-reviewed and published in English language. The key words used in searching the references were: MDCT angiography and coronary artery stents, MDCT imaging in coronary in-stent restenosis, MDCT assessment of coronary artery stent. The search was limited to reports on human subjects and excluded case reports, conference abstracts and review articles. The search of literature ranged from 1998 to 2007 (September 2007), as MDCT was first introduced into clinical practice in 1998 (14). In addition, the reference lists of identified articles were checked to obtain additional relevant articles. Prospective and retrospective studies were included if they met all of the following criteria: (a) patients undergoing both MDCT angiography and invasive catheter angiography examinations; (b) studies included at least 10 patients and must be performed with 16-or more detector row scanners (as earlier results performed with 4-detector row scanners showed very low visualization/visibility of coronary stents due to partial volume effects, beam hardening and cardiac motion artifacts); (c) assessment of coronary in-stent restenosis and occlusion was performed with MDCT angiography, and diagnostic value of MDCT angiography was addressed when compared to invasive catheter angiography in terms of sensitivity, specificity.

Data extraction

Data extracted by two reviewers was based on study design and procedure techniques. The reviewers looked for the following characteristics in each study: year of publication; number of participants in the study; mean age; mean heart rate; percentage of male patients affected; number of patients receiving β–blockage; type of imaging unit used for CT; scanning protocols; assessable stents in each study; location of stents implanted; diameter of the stents implanted, stent materials and diagnostic accuracy of MDCT angiography when compared to invasive catheter angiography with regard to the sensitivity and specificity in the detection of in-stent restenosis and occlusion, and main factors affecting the visualization/detection of coronary in-stent restenosis or occlusion. Moreover, the reviewers looked for the postprocessing methods used in each study with the aim of decreasing stent-related artifacts and improving spatial resolution.

Detection of in-stent restenosis

According to the literature that was reviewed, the method to determine coronary in-stent restenosis or occlusion was based mainly on contrast attenuation inside the stent lumen. In-stent restenosis was considered if the vessel distal to the stent implantation site was not visualized (occlusion) or massive low density area (or filling defects) inside the stent lumen was detected visually when compared with the reference vessel (the sites proximal and distal to the stent). Homogeneous enhancement (visually similar to the CT attenuation in the reference vessels) inside the stent lumen was considered to be normal or absent of in-stent restenosis. A decrease of more than

50% lumen diameter was used as the criterion for assessment of in-stent restenosis in the study.

Statistical analysis

All of the data was entered into SPSS 14.0 (SPSS Inc, Chicago, ILL) for analysis. The main focus of analysis was at the assessable stents, as most studies focused on this information. Sensitivity and specificity estimates for each study were independently combined across studies using a fixed effects model. Between-study heterogeneity of the sensitivity and specificity estimates was tested using the Mantel-Haenszel Chi-squared test with n-1 degree of freedom (n is the number of studies). Statistical hypotheses (2-tailed) were tested at the 5% level of significance.

Results

17 studies met the selection criteria and 15 were eligible for meta-analysis (9, 10, 15-29). Two studies were found to be cumulative addition of the previous cases to some extent. One of these studies was therefore excluded from the analysis (10). Another study was excluded from the analysis as it only dealt with MDCT detection of coronary stent patency without assessing the in-stent restenosis or occlusion (22). Table 1 lists patients' characteristics and scanning protocols in the studies reviewed. Of these 15 studies, eight were performed on 16-detector row scanners, and five were on 64-detector row scanners, and one on a 40-detector row scanner, while the remaining one was performed with a mixture of 16- and 64-detector row scanners.

The number of stents implanted in these studies ranged from 20 to 232 with a total number of 1333. The stents were deployed in the four main coronary branches in all of the studies, except in two studies in which stents were only implanted in the left coronary artery (16, 24). In five of 15 studies the stents were implanted in the saphenous vein graft in addition to the implantation in the coronary arteries.

Percentage of the assessable stents was variable among these studies with a mean value of 88% (95% CI: 80%, 95%). There was no significant difference between 16- and 64-detector row CT in the assessment of assessable stents (86% vs 90%) ($p>0.05$).

Table 2 provides information about stent materials used in the studies. Table 2 also provides details of the four coronary artery branches into which the stents were implanted. This information was available in 10 studies. Details of stent materials were only available in five studies, and most of the material used was made of stainless steel (more than 80%), while cobalt, tantalum and gold coated stents represented a small percentage of other materials.

The number of stents implanted in the four main coronary artery branches was provided in 10 of 15 studies, and the main stents vessels are left anterior descending and right coronary artery with pooled estimates of 44% (95% CI: 38%, 51%), 32% (95%CI: 27%, 38%), respectively. In contrast, left circumflex and left main coronary artery branches represented a small percentage of stents vessels, with pooled estimates being 18% (95%CI: 11%, 24%) and 3% (95%CI: 0.9%, 6%).

Coronary in-stent restenosis was found to be present in all studies, with prevalence less than 30% in most of the studies, except in one study which had a high prevalence of 49% (29), as shown in table 3. The mean prevalence was 18% with 95% CI being 13% and 24%.

Table 3 lists the sensitivity and specificity of MDCT angiography in the detection of coronary in-stent restenosis (>50%) reported in each study. Pooled sensitivity and specificity of MDCT angiography were 85% (95% CI: 78%, 90%) and 97% (95% CI: 95%, 98%), respectively, based on the assessable stents. Diagnostic accuracy of MDCT angiography with inclusion of non-assessable stents was reported in six studies, however, a meta-analysis was not performed because the results could not be adequately classified as a true positive or a true negative.

There was significant between-study heterogeneity in the sensitivity and specificity estimates in all analyses (table 3), with highly significant heterogeneity among the studies with respect to specificity ($p<0.001$). Therefore, we also performed a further analysis of these studies and nine of the 15 studies fit into the criterion demonstrating between-study homogeneity ($p>0.05$, inconsistency 0%). Figures 1-2 show the plots and tables of sensitivity and specificity of MDCT angiography compared to invasive catheter angiography in these nine studies. The pooled sensitivity and specificity of the nine studies were very close to those analysed with all 15 studies as demonstrated in table 3 and figures 1-2.

In addition to the overall diagnostic accuracy of MDCT angiography, comparison between 16- with 64-detector row CT in terms of the sensitivity and specificity for assessment of the coronary stent restenosis or occlusion was also made. This analysis showed that pooled sensitivity and specificity of MDCT angiography were 81% (95% CI: 69%, 93%) and 97% (95% CI: 93%, 100%) for 16-detector row CT; 87% (95% CI: 77%, 97%) and 95% (95% CI: 92%, 98%) for 64-detector row CT, respectively. Although a 64-detector row CT should be more accurate than a 16-slice one in the detection of coronary in-stent restenosis or occlusion, no significant difference was found when comparing these two types of scanners ($p>0.05$).

Factors affecting the visualization of coronary in-stent restenosis included motion artifacts, blooming artifacts, diameter of the coronary stents and severe calcification. Information about the effect of these factors on image visualization was available in 10 studies whilst detailed percentage of each factor causing the diagnostic difficulties was only available in two studies (19, 27). Therefore, it was not possible to perform a combined analysis of the effect of these factors on the diagnostic accuracy of MSCT angiography for detection of in-stent restenosis.

Discussion

The results show that MDCT angiography has good diagnostic accuracy for detection of coronary in-stent restenosis (sensitivity of 85%). With the current scanning technique (64 detector rows) MDCT has not reached the diagnostic performance to replace invasive catheter angiography in this aspect. However, with its particularly high specificity (97%), MDCT angiography could be used as a screening method for exclusion of coronary in-stent restenosis.

MDCT angiography in imaging of coronary stents differs from imaging of coronary artery tree as the detection of coronary in-stent restenosis is influenced not only by the cardiac motion, but also by the metal component of the stent. The presence of metal can lead to high-density artifacts, subsequently obscuring of a considerable part of the stent lumen. The material and design of the stent affects the amount of artifacts (the higher the density, the more apparent the artifacts). This effect is less apparent in larger vessels, such as the aorta and its abdominal branches, but does impair visualizations of the lumen in smaller vessels such as coronary arteries.

With earlier scanners like 4-deterctor row CT, the stent lumen was virtually invisible (7). With 16-and 64-detector row systems improved visualization has been reported in particular with stents having either a large diameter or thinner struts. Our results supported these findings to some extent. Studies performed with 16-and 64-detector row scanners when compared to 4-detector row scanners showed improvement in assessable coronary stents. However, the results must be interpreted with caution. Although the assessable segment is visualized in more than 80% in more than two-thirds of the studies reviewed using 16- or 64-detector row scanners, the results had a direct relationship with the assessable percentage and diameter of coronary artery stents implanted. This is shown in Table 3.

It was also seen that where the percentage of coronary artery stents with a diameter of more than 3 mm in the study was higher, there was a higher assessable rate or higher detection rate of coronary in-stent restenosis acquired with MDCT angiography. With 3.0 mm being used a threshold, the rate of evaluable stents or diagnostic value of MDCT angiography is relative low in stents with a diameter less than 3.0 mm. Inclusion of unassessable stents with a diameter of less than 3.0 mm in studies was found to result in unfavourable results, although this was only noted in six studies. Hence, future studies with inclusion of more stents with small diameters are required.

Commonly identified factors in MDCT angiography affecting the visualization of coronary artery disease include high heart rate, severe calcification in the arterial lumen, and small diameter of the vessels. When imaging the stents, the stent material itself and the strut thickness are two additional factors which contribute to the evaluation of coronary in-stent restenosis. Stents with a thin strut thickness were found to be able to be evaluated at a substantially higher rate than those with a thick strut thickness (25). Stent strut thickness was available in six studies, with criteria being selected to determine the thick struts (> 100 μm or140 μm) and thin strut (<100 μm or140 μm) in two studies (9, 25). In three studies, the number of patients treated with thick stent struts (> 100 μm) ranged from 42% to 90%. In these studies, this could be one of the main reasons leading to relatively low sensitivity of MDCT angiography for the detection of in-stent restenosis (9, 23, 25).

The results of this review show that the mean prevalence of in-stent restenosis was 18%. Restenosis may occur in up to 46% of bare-metal stents within the first 6 months after implantation, and many patients undergo repeat coronary angiography to rule out in-stent restenosis when chest pain recurs (19). This could result in additional invasive procedures with additional costs. The detection of in-stent restenosis following coronary artery stenting hence has significant clinical importance.

Drug-eluting stents could be an effective alternative to the bare-metal stents in terms of the overall incidence of post-procedural complications. It has been reported that the overall incidence of in-stent restensois and adverse cardiac events was significantly decreased with the use of drug-eluting stents when compared to bare-metal stents (30, 31). Of 15 studies that were reviewed, drug-eluting stents were used in nine studies. However, only a small percentage of the drug-eluting stents (8-28%) was used in eight studies when compared to those treated with the bare metal stents (72%). In the remaining study, the majority of stents implanted were drug-eluting ones (95%) (24).

Postprocessing of the original axial data is an important part for generation of images with good edge definition, improved spatial resolution and decreased stent-related artifacts. Of 15 studies reviewed, sharp reconstruction/convolution kernel was applied in half of the studies (table 3). Relatively higher sensitivity was achieved in most of the studies. A possible reason for quite low sensitivity in one study using edge-enhancing kernel is most likely to be due to the low percentage of large diameter coronary stents (58% of stents with a diameter of more than 3 mm) included in the study (19). Thus, the diagnostic accuracy of MDCT angiography in the detection of coronary stent restenosis or occlusion depends on multiple factors and postprocessing technique plays an important role in minimizing blooming artifacts in the reconstructed images.

Some limitations in our study do exist. First, the publication bias exists and may affect the results as non-English publications were excluded. Although it is apparent that more studies are being performed on 64-detector row scanners, it was difficult to include all of the potential studies in the analysis, especially those studies currently being undertaken or under review. Second, lack of uniform criteria of assessment is another limitation inherent in most of the studies reviewed. Not all of the studies provided complete data with regards to the type, diameter of the coronary stents implanted. Thus, we contacted several investigators to obtain clarification or additional data that enhanced our analyses. Third, a limitation of pooled sensitivities and specificities is that different positive criteria used in individual studies are not considered. Between-study heterogeneity is significant, however, heterogeneity is not necessarily a limitation in meta-analysis (32), and it provides a key opportunity to show the consistent performance of the method.

In conclusion, the meta-analysis showed that the latest MDCT angiography (16 or more detector rows) provides moderate sensitivity and high specificity for the detection of coronary in-stent restenosis when compared to invasive catheter angiography. The diagnostic performance of MDCT angiography was mainly influenced by the type of stents implanted, diameter of the coronary stents, and thickness of the stents struts. Based on the current available results, invasive catheter angiography still remains the gold standard technique for follow-up of coronary in-stent restenosis. With the high specificity, MDCT angiography could be used as a reliable technique to rule out the presence of in-stent restenosis. Further studies performed with 64-detector row or dual source CT should focus on using improved imaging techniques to reduce artifacts resulting from the implanted stents.

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