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ORIGINAL ARTICLE

Evaluation of Nitroglycerin Premedication on the Arterial Luminal Diameter and Branches of Coronary Arteries on 64-Multidetector Computed Tomography Angiography

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Background: The 64-multidetector computed tomography (64-MDCT) has developed into a mature clinical tool to detect coronary artery disease. This 64-MDCT system permits cross-sectional and longitudinal imaging of the coronary arteries with a high spatial and temporal resolution. However, small vessels, side branches and the distal portions of the main coronary arteries are not always optimally visualized.

Purpose: The aim of this study was to evaluate the effect of nitroglycerin (NTG) on lumen diameters and the number of visualized side branches of the coronary arteries on 64-MDCT. We also assessed whether NTG would affect the quality of the images of the coronary arteries obtained by 64-MDCT.

Methods: Sixty-seven patients were randomized and divided into two groups: Group C (31 patients, no sublingual NTG) and Group N (36 patients, sublingual NTG given before the scan). We measured the lumen diameter of the coronary artery and visibility of the side branches by using the 64-MDCT system and also evaluated the image quality by using the scores.

Results: The cardiac 64-MDCT images of these patients showed that the average diameters of the proximal segments in the right coronary artery, left main artery, left anterior descending coronary artery, and left circumflex coronary artery were 4.1 ± 0.7 mm, 3.9 ± 0.6 mm, 3.6 ± 0.7 mm, and 3.4 ± 0.6 mm, respectively, in Group N and 3.0 ± 0.5 mm, 3.1 ± 0.6 mm, 2.8 ± 0.5 mm, and 2.7 ± 0.5 mm, respectively in Group C. In addition, the scores for visibility and image quality for the side branches in Group N were significant higher than for those in Group C.

Conclusion: Our study indicates that CT coronary angiography using 64-MDCT with NTG administration produces images of diagnostically acceptable quality in all coronary segments. Thus, NTG might be recommended for routine 64-MDCT coronary angiography examinations.

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1. Introduction

Since their discovery approximately 130 years ago, organic nitrates have served as effective therapeutic agents to relieve the symptoms of angina pectoris and to prevent their occurrence.[1] The physiological mechanisms of action of the organic nitrates are diverse; thus, these drugs can benefit patients in a variety of cardiovascular diseases, including coronary artery disease, congestive heart failure, and acute myocardial infarction.[2,3] Among these compounds, the most well known is nitroglycerin (NTG), which provides an excellent therapeutic profile. NTG is generally rapidly acting, safe, and free of serious side effects.[4] The administration of NTG has long been used to obtain maximal dilatation of the epicardial coronary arteries during conventional coronary angiography.[5] More recently, 64-multidetector computed tomography (64-MDCT) has developed into a mature clinical tool to detect coronary artery disease.[6] This 64-MDCT system permits cross-sectional and longitudinal imaging of the coronary arteries with a high spatial and temporal resolution. Decramer et al[7] evaluated

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the coronary lumen diameter and the number of septal branches visualized by using 64-MDCT and obtained excellent accuracy. However, small vessels and side branches and the distal portions of the main coronary arteries are not always optimally visualized.[8] The aim of this retrospective study was to evaluate the effect of NTG on lumen diameters and the number of visualized side branches of coronary arteries on 64-MDCT. In addition, we assessed whether NTG would affect the quality of the images of the coronary arteries obtained by 64-MDCT.

2. Materials and Methods

Six hundred seventy-eight patients referred by the cardiologist in our hospital underwent 64-MDCT angiography of the coronary artery in our cardiac image center between January and December 2007. All coronary artery CT scans were performed using a 64-MDCT scanner with a 0.35-seconds rotation time (Volume Computed Tomography Light Speed CT/I; GE Medical Systems, Milwaukee, WI, USA). We scanned all patients after injection with about 70–80 mL contrast medium (Optiray; Mallinckrodt, St Louis, MO, USA) followed by an injection of 40 mL saline. All patients were administered 20 mg inderal orally 30 minutes before the CT scan. Depending on the affinity of the radiologists, some patients were also given 0.6 mg sublingual NTG 5 minutes before the scan. We selected the 445 patients who were aged 40–60 years from these 678 patients. From these 445 patients, 378 patients were excluded because they were found to have had significant calcification, stenosis, and anomalies in the coronary artery. The remaining 67 patients (36 men and 31 women, mean age: 57.8 years) comprised our study subjects. We divided the patients into two groups according to whether they had taken NTG before the scan (Group N: 20 men, 16 women, Figure 1), or had not (Group C: 16 men, 15 women, Figure 2). When reviewed their images, the reviewers did not know which group these patients belong to. Except for the use of NTG, the scanning protocols for the two groups were similar.

Figure 1 The diameters of vessels dilation and visibility increasing of branch numbers caused by taking NTG. NTG = nitroglycerin.

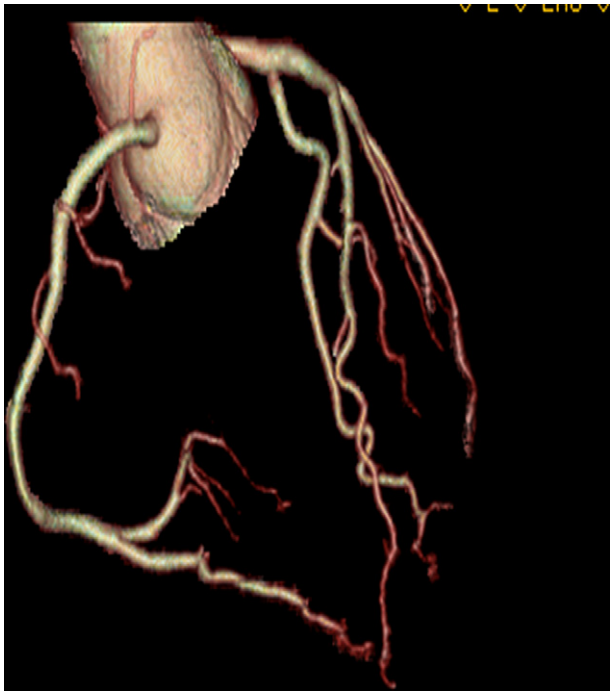

Figure 2 Without NTG, the diameters of vessels dilation and visibility increasing of branch numbers cannot be obviously seen. NTG = nitroglycerin.

2.1. Measurement of the lumen diameter of the coronary artery and visibility of the side branches

The 64-MDCT data were transferred from the scanner to the ADW (Advantage Workstation; GE Medical Systems, Milwaukee, WI, USA) for analysis of the images. One reviewer measured the diameters of the right coronary artery (RCA), left main artery (LMA), left anterior descending coronary artery (LAD), and left circumflex coronary artery (LCX). Measurements of the coronary artery diameters were taken about 0.5 cm distal to the origin of the artery in a plane perpendicular to a curved multiplanar reconstruction along the long axis of the vessel. We used a scoring system to represent the visibility of the side branches: one visible side branch was scored as 1 point and so on. The visibility scores for the side branches included two parts: the first order branches mean the branches of the RCA or left coronary artery, and the second order branches mean the branches of the first order branches.

2.2. Image quality

The quality of the images of the three main arteries was evaluated by two reviewers, Dr Chi-Ming Lee and Dr Hung-Jung Wang. Quality scores were assigned as follows: 4 points when the images of the three coronary arteries were of good quality with smooth outlines; 3 points when the images of two coronary arteries were of good quality with smooth outlines; 2 points when the image of one coronary artery was of good quality with a smooth outline, and 1 point when the images of all the three coronary arteries were of poor quality with uneven outlines. The scores from the two reviewers were combined, with a total score of 6–8 points indicating good image quality.

2.3. Statistical analysis

Data are reported as mean with standard deviation. These data between the two groups of patients were analyzed by using the

unpaired t test. A p value less than 0.05 was considered statistically significant.

The authors had full access to the data and took responsibility for its integrity. All authors have read and agree to the manuscript as written.

3. Results

The clinical characteristics of patients were listed in Table 1. No statistically significant differences between mean ages, sex, heart rate, height, weight, and body mass index were found between two groups before scanning. The differences in the lumen diameters between Groups N and C were statistically significant with the average lumen diameters of the RCA, LMA, LAD, and LCX in Group N markedly larger than in Group C (4.1 ± 0.7 mm, 3.9 ± 0.6 mm, 3.6 ± 0.7 mm, and 3.4 ± 0.6 mm *vs.* 3.0 ± 0.5 mm, 3.1 ± 0.6 mm, 2.8 ± 0.5 mm, and 2.7 ± 0.5 mm, respectively) as shown in Table 2. Similarly, the visibility scores (shown in Table 3) for the side branches were higher in Group N, with scores for the first order branches of RCA, LAD, and LCX of 7.4, 5.4, and 4.3 in Group N versus 5.3, 3.8, and 2.5 in Group C. The visibility scores for second order branches of the RCA, LAD, and LCX in Group N were 2.1, 1.4, and 0.8; whereas those in Group C were 1.1, 0.5, and 0.5. Seventy-two percent of the patients in Group N had a total image quality score between 6 and 8, whereas 45.2% of the patients in Group C had scores of 6 or higher ($p < 0.05$). No major side effects were observed in the study apart from a mild headache reported by 12 patients.

4. Discussion

Since the introduction of 64-MDCT as a noninvasive tool for the depiction of coronary arteries, the clinical value of CT coronary angiography has been evaluated in several studies.[9,10] The 64-MDCT with the intravenous injection of contrast agent permits the visualization of the coronary artery lumen and the detection of stenoses. However, previous 64-MDCT investigations had revealed two major limitations: coronary artery motion frequently is not sufficiently suppressed, causing effects on the visibility and stenosis assessment of side branches.[11]

NTG had been traditionally thought of as an endothelium-independent vasodilator.[12] Biochemically, NTG is thought to exert its action through the liberation of nitrite oxide in the vasculature.[13] However, the metabolic pathways by which this is accomplished are still not completely understood. In a study by Giesler et al,[14] the image quality of CT coronary angiography using 16-MDCT was found to be improved by NTG treatment, which produced 95.8% diagnostically acceptable coronary segments compared with 86.3% without NTG treatment. These authors also demonstrated that the most prominent improvement of image quality with NTG treatment was observed in the RCA. In our retrospective review of our data bank, we found that more side branches could be visualized when patients received NTG before 64-MDCT scanning. The visibility scores for the side branches in Group N were 1.4–2.8 times higher than those in Group C. The administration of NTG also led to a significant increase in lumen diameter in the RCA, LMA, LAD, and LCX (Table 2). These effects have the potential to improve the reproducibility and accuracy of 64-MDCT for the detection of coronary artery stenoses. Dewey et al[11] retrospectively selected 950 patients who underwent 4-slice, 16-slice, or 64-slice CT with oral NTG administration. They found that a significant difference in the size of the proximal coronary arteries was noted in the 16-slice and 64-slice CT. The fact that their findings differ from the results obtained by Hackenbroch et al,[15] who found no significant changes with intravenous nitrate in magnetic resonance imaging ($3.0 \times 0.7 \times 0.5$ mm^3), might be explained by the smaller voxel size of MDCT that allows the detection of diameter changes in this smaller size range.

In a study by Decramer et al,[7] 42 patients were prospectively included in a 64-MDCT study; 21 were examined without sublingual NTG (Group A), and 21 were examined after the administration of sublingual NTG (Group B). They found the lumen diameters and the average volumes were significantly larger in Group B than in Group A. The number of side branches visualized in Group B was significantly greater than in Group A (the sinoatrial branch was present in 67% of group A compared with 95% of group B; and the conus branch was present in 33% of Goup A compared with 62% of Group B). They also found that NTG led to a significant increase in volume in both the RCA and the LAD. In a study by Hoffman et al,[16] subjects were divided into control and NTG groups and their coronary aniographies examined by 64-MDCT. The results showed that the average diameters of the LMA, LAD, LCX, and RCA increased 12%, 17%, 19%, and 21%, respectively, for the group with NTG compared with the control group. In a study by Klass et al,[17] they demonstrated that sublingual administration of NTG before coronary angiography results in improved diagnostic image quality because of a significant dilation and improved intraluminal contrast agent density of the peripheral vessels. In addition, they also chose the posterior descending artery to analyze image quality. They found that the image quality scale of NTG group and NTG without group were 3.9–4.0 and 1.8–2.6 ($p < 0.001$), respectively. In a study by Chun et al,[18] 46 patients received a sublingual NTG 1 minute before 16-slice CT scanner. They found that based on the luminal size of each segment, diagnostic accuracy in the NTG group was significantly higher for proximal segments than in the non-NTG group (96.7% *vs.* 89.7%). These results were similar to ours in which the average diameters of the LMA, LAD, LCX, and RCA were increased 26%, 25%, 26%, and 36%, respectively, in the group with NTG compared with the control group. We found the effects of NTG were greater in the RCA than in the other vessels. Although we could find no reports in the literature of a contribution by the RCA to better image quality, our data and those of Decramer et al[7] and Hoffman et al[16] demonstrated that NTG led to a significant increase in volume or diameter in the RCA. Thus, we conclude that the dilation of the RCA diameter could be associated with the improvement in image quality, although further studies are needed to confirm such a relationship. In addition, we found that image quality could be improved markedly after NTG treatment as judged by the fraction of patients with good image quality scores. However,

Table 1 Clinical characteristics of patients

Characteristics	Group C	Group N	p
Age (yr)	58.6 ± 2.4	56.4 ± 1.9	NS
Sex (male:female)	16:15	20:16	NS
Heart rate (beats/min)	59.6 ± 5.6	61.2 ± 4.2	NS
Weight (kg)	69.2 ± 8.1	71.0 ± 6.6	NS
Height (cm)	167.4 ± 4.9	166.2 ± 8.7	NS
Body mass index (kg/m^2)	24.7 ± 4.5	25.7 ± 3.9	NS

NS = not significant.

Table 2 Differences in diameters (mm) of the coronary artery segments between Groups C and N

	RCA	LMA	LAD	LCX
Group C	3.0 ± 0.5	3.1 ± 0.6	2.8 ± 0.5	2.7 ± 0.5
Group N	4.1 ± 0.7	3.9 ± 0.6	3.6 ± 0.7	3.4 ± 0.6
p	< 0.05	< 0.05	< 0.05	< 0.05
Increase (%)	36.6	25.8	28.6	25.9

Group N received sublingual nitroglycerin and Group C did not receive nitroglycerin. LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LMA = left main artery; RCA = right coronary artery.

Table 3 Differences in visibility scores for side branches of the coronary artery between groups C and N

	RCA		LAD		LCX	
	1st order branches	2nd order branches	1st order branches	2nd order branches	1st order branches	2nd order branches
Group C	5.3 ± 1.8	1.1 ± 1.2	3.8 ± 1.6	0.5 ± 0.7	2.5 ± 1.5	0.5 ± 0.8
Group N	7.4 ± 2.7	2.1 ± 1.4	5.4 ± 1.7	1.4 ± 1.5	4.3 ± 1.9	0.8 ± 0.9
p	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	NS

Group N received sublingual nitroglycerin and Group C did not receive nitroglycerin.
LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; NS = not significant; RCA = right coronary artery.

Pfister et al[19] demonstrated that the form of administration of NTG will affect the vasodilator efficiency. They noted that sublingual NTG (organic form) may be more efficacious than other inorganic nitrates and also suggested that the form of administration NTG cannot be ignored when using it in 64-MDCT examination.

In conclusion, our study indicates that CT coronary angiography using 64-MDCT with NTG administration produces images of diagnostically acceptable quality in all coronary segments. Thus, NTG might be recommended for routine 64-MDCT coronary angiography examinations.

References

1. Fung HL. Biochemical mechanism of nitroglycerin action and tolerance: Is this old mystery solved? *Annu Rev Pharmacol Toxicol* 2004;**44**:67–85.
2. Pi XC, Yan C, Kim D, Chen JY, Berk BC. Differential expression of genes grom nitrate-tolerant rat aorta. *J Vasc Res* 2002;**39**:304–10.
3. Ignarro LJ. After 130 years, the molecular mechanism of action of nitroglycerin is revealed. *Proc Natl Acad Sci USA* 2002;**99**:7816–7.
4. Fung HL. Clinical pharmacology of organic nitrates. *Am J Cardiol* 1993;**72**:9C–13C.
5. Chen Z, Zhang J, Stamler JS. Identification of the enzymatic mechanism of nitroglycerin bioactivation. *Proc Natl Acad Sci USA* 2002;**99**:8306–11.
6. Caussin C, Larchez C, Ghostine S, Pesenti-Rossi D, Daoud B. Comparison of coronary minimal lumen area quantification by sixty-four-slice computed tomography versus intravascular ultrasound for intermediate stenosis. *Am J Cardiol* 2006;**98**:871–6.
7. Decramer I, Vanhoenacker PK, Sarno G, Van-Hoe L, Bladt O, Wijns W, Parizel PM. Effects of sublingual nitroglycerin on coronary lumen diameter and number of visualized septal branches on 64-MDCT angiography. *Am J Roentgen* 2008;**190**:219–25.
8. Nieman K, Cademartiri F, Lemos PA, Raaijmakers R, Pattynama PM. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. *Circulation* 2002;**106**:2051–4.
9. Hamon M, Biondi-Zoccai GG, Malagutti P. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a meta-analysis. *J Am Coll Cardiol* 2006;**48**:1896–910.
10. Schoepf UJ, Becker CR, Ohnesorge BM, Yucel EK. CT of coronary artery disease. *Radiology* 2004;**232**:18–37.
11. Dewey M, Hoffman H, Hamm B. Multislice CT coronary angiography: effect of sublingual nitroglycerin on the diameter of coronary arteries. *Rofo* 2006;**178**:600–4.
12. Chung SJ, Fung HL. Identification of the subcellular site for nitroglycerin metabolism to nitric oxide in bovine coronary smooth muscle cells. *J Pharmacol Exp Ther* 1990;**253**:614–9.
13. Tseng CM, Tabrizi-Fard MA, Fung HL. Differential sensitivity among nitric oxide donors toward ODQ-mediated inhibition of vascular relaxation. *J Pharmacol Exp Ther* 2000;**292**:737–42.
14. Giesler T, Baum U, Ropers D. Noninvasive visualization of coronary arteries using contrast enhanced multidetector CT: influence of heart rate on image quality and stenosis detection. *Am J Roentgen* 2002;**179**:911–6.
15. Hackenbroch M, Meyer C, Schmiedel A, Hofer U, Flacke S, Kovacs A, Tiemann K, et al. The value of applying nitroglycerin in 3D coronary MR angiographie with real-time navigation technique. *Rofo* 2004;**176**:1133–41.
16. Hoffman MH, Shi H, Manzke R. Noninvasive coronary angiography with 16-detector row CT: effect of heart rate. *Radiology* 2005;**234**:86–97.
17. Klass O, Mutlu S, Hohl K, Feuerlein S, Jeltsch M, Brambs HJ, Hoffman H. Multidetector computed tomography coronary angiography: sublingual nitroglycerine improves image quality significantly because of peripheral coronary vasodilatation. *J Comput Assist Tomogr* 2009;**33**:199–203.
18. Chun EJ, Lee W, Choi YH, Koo BK, Choi SI, Jae HJ, Kim HC, et al. Effects of nitroglycerin on the diagnostic accuracy of electrocardiogram-gated coronary computed tomography angiography. *J Comput Assist Tomogr* 2008;**32**:86–92.
19. Pfister M, Seiler C, Fleisch M, Gsbel H, Liischer T, Meier B. Nitrate induced coronary vasodilatation: differential effects of sublingual application by capsule or spray. *Heart* 1998;**80**:365–9.