Attenuation Drop of Intra-Mural Coronary Segment Observed at Diastolic Phase of Coronary CT Angiography Predicts Significant Systolic Compression of Myocardial Bridge

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Objective: To study the diagnostic value of percentage attenuation drop measured by coronary computed tomography angiography (CTA) for identifying significant dynamic compression of myocardial bridge (MB).

Materials and Methods: Patients with MB-confirmed vessels who underwent retrospectively electrocardiogram-gated coronary CTA were reviewed. The average attenuation of the MB segment ($\text{attenuation}_{\text{MB}}$) as well as the segment from the vessel ostium to MB entrance point ($\text{attenuation}_{\text{proximal}}$) was calculated. The difference in Hounsfield unit between attenuation proximal and $\text{attenuation}_{\text{MB}}$ was divided by $\text{attenuation}_{\text{proximal}}$ to obtain the percentage attenuation drop of the mural coronary artery. The percentage attenuation drop of MB vessel, length of MB, and depth of MB were measured and correlated with the presence and degree of dynamic compression observed at the invasive coronary angiography. Systolic compression $\geq 50\%$ was considered significant.

Results: 135 patients with CTA-confirmed MB lesions were included. The percentage of attenuation drop of MB segment ($20.2 \pm 11.9\%$ vs. $7.7 \pm 7.9\%$, $p < 0.001$) as well as MB length (25.4 ± 11.6 mm vs. 17.3 ± 6.2 mm, $p = 0.001$) was largest in the subgroup of significant dynamic compression and smallest in the subgroup of no dynamic compression. ROC curve analysis determined the best cutoff value of percentage of attenuation drop as 15% (area under curve = 0.75, 95% confidence interval = 0.668–0.82, $p < 0.001$), which yielded high diagnostic accuracy (73.3%, 99/135).

Conclusion: The percentage attenuation drop of the MB segment significantly correlated with the extent of dynamic compression of the MB. Percentage attenuation drop $\geq 15\%$ (cutoff value) has high diagnostic accuracy (73.3%, 99/135) for identifying significant dynamic compression of a MB.

Key words Coronary artery disease · Multidetector computed tomography · Angiography.

Received: January 6, 2018

Revised: March 5, 2018

Accepted: March 29, 2018

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INTRODUCTION

Myocardial bridge (MB) is a common congenital anomaly in which an epicardial portion of coronary artery is completely

covered by the myocardium [1]. From angiographic and autopsy studies, this anatomic variant is almost exclusively observed in the left anterior descending artery [2,3]. Although the clinical outcomes are considered benign in most patients with MB [4], MB is potentially associated with myocardial ischemia, acute coronary syndromes, coronary spasm, arrhythmia, and sudden death [5-11].

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The MB detection rate varies significantly between the different imaging modalities of coronary computed tomography angiography (CTA) and invasive coronary angiography (ICA). Coronary CTA usually reveals a much higher incidence of MB than ICA [12-16] due to the capability of coronary CTA to detect MB without the presence of systolic compression. The clinical significance of myocardial bridging lies in related regional hemodynamic changes caused by dynamic compression. It is of clinical importance to non-invasively differentiate compression-related and non-compression related MB by coronary CTA to determine proper treatment strategies. Traditional morphological parameters measured on coronary CTA have been studied, such as MB length and depth, but the value of any single parameter for predicting significant dynamic compression remains unclear [12,13]. Myocardial ischemia caused by MB is not only related to systolic vascular compression but also to persistent diastolic filling dysfunction [17]. We hypothesized that persistent diastolic filling dysfunction might lead to the attenuation drop of the mural coronary artery segment observed in the diastolic phase of coronary CTA. Therefore, we aimed to study the diagnostic performance of a series of CTA parameters, including attenuation drop of the mural coronary artery, to identify dynamic compression of MB.

MATERIALS AND METHODS

Patient population

Institutional Review Board approval was obtained for this retrospective study (IRB No. 0811214), and informed consent was waived. Between December 2012 and June 2015, consecutive patients who underwent coronary CTA for evaluation of chest discomfort were retrospectively reviewed. The inclusion criteria were 1) CTA revealed the presence of MB and 2) retrospective electrocardiogram (ECG)-gated acquisition was employed and artifact was absent in both diastolic and systolic phases. Exclusion criteria were 1) CTA revealed the absence of MB, 2) target vessel (MB vessel) had concomitant obstructive coronary artery disease (defined as diameter stenosis $\geq 50\%$ diagnosed by CTA, which might also cause lumen attenuation), 3) previous history of attempted coronary revascularization of target vessel (percutaneous coronary intervention or bypass surgery), 4) target vessel was diffusely calcified (defined as circumferential calcification with length ≥ 5 mm), 5) artifact was present in either diastolic or systolic phases, or 6) coronary CTA was uninterpretable due to poor image quality.

Scan protocol of coronary CTA

A 128-slice multidetector CT (Definition AS, Siemens Medical Solutions, Forchheim, Germany) was employed for scanning. A β -blocker (25–75 mg) was administered orally 1 hour

prior to the examination in patients with heart rate >65 bpm. Nitroglycerin was given sublingually in all patients. A bolus of contrast media (Iopamidol, Isovist, 370 mg iodine/mL, Schering AG, Berlin, Germany) was injected into the antecubital vein at a rate of 4.5–5 mL/s followed by a 20–40 mL saline flush using a dual-barrel power injector (Tyco, Cincinnati, OH, USA). The amount of contrast media was determined according to the patient's body weight and scan time. A test bolus was first injected and the region of interest was placed within the ascending aorta to determine a proper delay time, which was defined as 4s plus the peak time of the ascending aorta. Retrospective ECG-gated CTA was performed with collimation= 64×0.6 mm, reconstructed slice thickness= 0.6 mm, reconstructed slice interval= 0.5 mm, and rotation time= 300 ms. Pitch and current ECG were modified and the effective current was set as 200 mA (ECG-dependent dose modulation technique was applied, full dose during R-R interval of 30–80%). Tube voltage was 120 kVp.

CTA image reconstruction and analysis

Data was transferred to an offline workstation (Syngo, Siemens) for further analysis. The coronary CTA (CCTA) dataset was reconstructed at 5% intervals from 30% of R-R interval to 80% of R-R interval. The end-systolic phase (30% of R-R interval to 40% of R-R interval) and mid-diastolic phase (65% of R-R interval to 80% of R-R interval) with the best image quality were manually selected and used for further assessment. Axial images, cross-sectional view, curved planar reformation (CPR), and multiplanar reformation (MPR) images were available for evaluation.

MB was diagnosed at coronary CTA if a coronary segment was completely surrounded by myocardium on axial, MPR, and cross-sectional images. The total MB length was measured on CPR at best projection view from the entrance point to the exit point. Depth of the MB was determined by measuring the maximal thickness of overlying muscle on cross-sectional images. When MB was superficially present with the overlying myocardium thinner than or equal to 1 mm, a thickness of 1 mm was recorded for further quantitative analysis. All lumen attenuation measurements were made on cross-sectional images of the mid-diastolic phase by manually drawing the region of interest (size= 2 mm^2) with careful exclusion of vessel calcification. The luminal radiological attenuation [Hounsfield unit (HU)] was measured at 5 mm intervals from the ostium of an epicardial artery to the level of the MB exit point. Average attenuation of the MB segment (attenuation_{MB}) as well as the segment from the vessel ostium to MB entrance point (attenuation_{proximal}) were calculated. The difference in HU between attenuation_{proximal} and attenuation_{MB} was divided by attenuation_{proximal} to obtain the percentage attenuation drop of mural coronary artery. MB lesions were divided into three subgroups according to the extent of systolic compression as determined by end-systolic phases of CTA im-

ages: absence of systolic compression, presence of mild systolic compression (defined as lumen narrowing <50% in end-systolic phase), and presence of significant systolic compression (defined as lumen narrowing $\geq$ 50% in end-systolic phase).

Two experienced radiologists who were blinded to clinical histories independently analyzed the lesions. Any disagreement between the two observers was resolved by consensus.

Statistical analysis

Statistical analysis was performed using commercially available statistical software (SPSS, version 13.0; SPSS Inc., Chicago, IL, USA and MedCalc Statistical Software version 15.2.2; MedCalc Software bvba, Ostend, Belgium). Quantitative variables were expressed as mean $\pm$ standard deviation. T-test and Pearson test were used for normally distributed data while Mann-Whitney U-test was used for data that were not normally distributed. Continuous and categorical variables were compared by the Mann-Whitney U or χ^2 test. Fisher's exact test was used to make comparison of proportions. Univariate statistical tests were performed to identify variables associated with dynamic compression-present lesions. Pearson correlation analysis was also performed to compare the degree of systolic compression with attenuation drop, MB depth, and MB length assessed with coronary CTA. The best cut-offs of various parameters were determined by the maximum sum of sensitivity and specificity of receiver operating characteristic (ROC) curve analysis. The sensitivity, specificity, positive predictive value, and negative predictive value of best cut-offs for percentage attenuation drop, MB length, and MB depth for identifying significant dynamic compression were tested. A 2-tailed $p < 0.05$ was considered statistically significant.

RESULTS

Clinical characteristics

A total of 4916 patients undergoing coronary CTA between December 2012 and June 2015 were eligible for evaluation. As shown in Fig. 1, 4781 patients were excluded according to exclusion criteria. Therefore, 135 patients [mean age: 60.2 ± 12.5 years, range: 22 to 91 years, 65 males (mean age: 57.5 ± 14.7 years, range 22 to 91) and 70 females (mean age: 62.6 ± 9.4 years, range 37 to 85)] were finally included in the study. The dose length product of CCTA was 571.1 ± 54.4 mGy*cm (range: 427 to 757 mGy*cm). The mean contrast used for CCTA was 80.7 ± 8.6 mL (range 65 mL to 105 mL). Detailed demographic data are given in Table 1.

Correlation of CTA-based parameters with significant MB dynamic compression

Three CTA-based parameters, percentage attenuation drop

Fig. 1. Flow chart of patient inclusion and exclusion. CTA: computed tomography angiography, MB: myocardial bridge, CAD: coronary artery disease.

of MB segment, MB length, and MB depth, were measured to test their correlation with significant MB dynamic compression as assessed by quantitative CTA evaluation. Representative cases are shown in Figs. 2 and 3. The percentage attenuation drop of the MB segment was largest in the subgroup with significant dynamic compression and smallest in the subgroup with no dynamic compression (Table 2). A similar discrepancy between the 3 subgroups was also observed for MB length (Table 2). In contrast, MB depth was similarly distributed across the three subgroups and only a minor insignificant difference was noted between the different subgroups (Table 2).

Table 1. Demographic data

	All patients (n=135)	MBs without dynamic compression (n=41)	MBs with insignificant dynamic compression (n=43)	MBs with significant dynamic compression (n=51)	p value
Age (years)	60.2±12.5	60.4±13.1	59±12.6	61±12.1	0.544
Male	65 (48.1)	17 (41.5)	19 (44.2)	29 (56.9)	0.279
Diabetes mellitus	18 (13.3)	6 (14.6)	8 (18.6)	4 (7.8)	0.298
Hypertension	52 (38.5)	18 (43.9)	15 (34.9)	19 (37.3)	0.678
Smoking	37 (27.4)	11 (26.8)	13 (30.2)	13 (25.5)	0.872
Hyperlipidemia	35 (25.9)	9 (22)	11 (25.6)	15 (29.4)	0.718
MB locations					
LAD	132 (97.8)	38 (92.7)	43 (100)	51 (100)	0.030
RCA	3 (2.2)	3 (7.3)	0 (0)	0 (0)	0.030

Data are presented as mean±standard deviation or number (%). Significant dynamic compression of MB was defined as systolic compression ≥50%, as determined by quantitative coronary CT angiography. MB: myocardial bridge, LAD: left anterior descending, RCA: right coronary artery

Fig. 2. Representative case of MB with dynamic compression. (A) CPR image of mid-diastolic phase showed presence of MB at middle LAD (black arrowhead). MB depth and length were measured as 2.8 mm and 19.1 mm, respectively. Percentage attenuation drop of MB segment was 28%. (B) CPR image of end-systolic phase identified significant compression (>90%) of MB segment (black arrowhead). (C) VR image confirmed evident presence of MB at middle LAD (black arrowhead). CPR: curved planar reformation, LAD: left anterior descending, MB: myocardial bridge, VR: volume rendering, HU: Hounsfield unit.

Diagnostic performance of CTA-derived parameters for identifying MB dynamic compression

ROC curve analysis was performed to determine the best cut-offs of each CTA-derived parameter for identifying MB dynamic compression. Percentage attenuation drop was found to have the largest area under curve in ROC curve analysis (Table 3, Fig. 3). In addition, it yielded the highest diagnostic accuracy (73.3%, 99/135) among all parameters when using 15% as the cut-off value (Table 3).

DISCUSSION

The current study has two major findings. First, the percent-

age attenuation drop of MB segment significantly correlated with the extent of dynamic compression of MB. Second, percentage attenuation drop ≥15% (the best cutoff value) has high diagnostic accuracy (73.3%, 99/135) to identify significant dynamic compression of MB.

MB is a common anatomic anomaly identified by coronary CTA in routine practice and is seen in as many as 40–80% of cases on autopsy [2,3]. Although MB is generally considered a benign anomaly, it may be associated with clinical manifestations that have been linked to dynamic compression [5–11]. The treatment strategy is guided by the presence of reduced myocardial perfusion, which is closely related to extent of dynamic compression [18,19]. Therefore, it is clinically important to iden-

Fig. 3. ROC curve analysis of CTA-derived parameters for identifying significant dynamic compression of MB*. Percentage attenuation drop (A) showed largest AUC and best diagnostic performance compared with MB depth (C) and MB length (B). *Significant dynamic compression of MB was defined as systolic compression $\geq 50\%$ as determined by quantitative coronary CTA. AUC: area under curve, CI: confidence interval, CTA: computed tomography angiography, MB: myocardial bridge, ROC: receiver operating characteristic.

Table 2. Comparison of CTA-derived parameters in patients with or without dynamic compression of MB

	All MBs (n=135)	MBs without dynamic compression (n=41)	MBs with insignificant dynamic compression (n=43)	MBs with significant dynamic compression (n=51)	p value
Percentage attenuation drop (%)	14 $\pm$ 11.6	7.7 $\pm$ 7.9	12.6 $\pm$ 10.6	20.2 $\pm$ 11.9	<0.001
MB length (mm)	21.5 $\pm$ 10.2	17.3 $\pm$ 6.2	20.9 $\pm$ 10.2	25.4 $\pm$ 11.6	0.001
MB depth (mm)	1.5 $\pm$ 1.1	1.3 $\pm$ 1.1	1.5 $\pm$ 1	1.8 $\pm$ 1.1	0.070

Significant dynamic compression of MB was defined as systolic compression $\geq 50\%$, as determined by quantitative coronary CT angiography. CTA: computed tomography angiography, MB: myocardial bridge

Table 3. ROC curve analysis of CTA-derived parameters for identifying significant dynamic compression of MB

	AUC	95% CI	p value	Best cutoff value	Diagnostic accuracy (%)	Sensitivity (%)	Specificity (%)
Percentage of attenuation drop	0.750	0.668–0.820	<0.001	>15%	73.3	68.6	75
MB length	0.676	0.590–0.754	<0.001	>23.2 mm	68.1	53	76.2
MB depth	0.607	0.519–0.690	0.031	>0.9 mm	55.6	72.5	44

Significant dynamic compression of MB was defined as systolic compression $\geq 50\%$, as determined by quantitative coronary CT angiography. AUC: area under curve, CTA: coronary computed tomography angiography, MB: myocardial bridge, ROC: receiver operating characteristic, CI: confidence interval

tify the presence of significant dynamic compression to select proper candidates for medical treatment.

ICA is regarded as the reference standard for assessing MB dynamic compression due to its ability for reliable quantitative analysis. However, it is neither reasonable nor practical to use such an invasive imaging modality merely to quantify MB compression in patients without coronary artery disease. Coronary CTA has been proven to be more sensitive than ICA for detection of MB due to its ability to visualize the intra-mural course of coronary arteries [12–16]. However, determination of compression extent requires artifact-free images of end-systolic phases, which are sometimes not available with low-dose prospective acquisition [12]. In addition, dynamic compression was only present in 23–46% of cases with CTA-detected MB [12,13]. Therefore, the value of traditional CTA evaluation of MB is limited.

This current study explored the use of a novel parameter, percentage attenuation drop of MB segment, to evaluate dynamic compression of MB. Compared with traditional morphological parameters such as MB depth and MB length, the attenuation drop percent showed superior diagnostic performance for detecting significant dynamic compression of MB. The underlying mechanism for altered vessel attenuation in such circumstances is potentially explained by the following hypothesis. Myocardial ischemia caused by MB is not only related to systolic vascular compression but also to persistent diastolic filling dysfunction [17], which might give rise to incomplete filling of contrast media in the bridged segment in both systolic and diastolic phases. Therefore, the decreased lumen attenuation of the MB segment could potentially persist throughout the whole cardiac cycle and result in a larger percentage attenuation drop

in the diastolic phase if significant dynamic compression is present. Two recent studies revealed that intraluminal attenuation decreased with diminution of vessel diameter, and transluminal attenuation gradient (TAG) does not provide incremental diagnostic value over CCTA alone for diagnosing ischemia-related coronary lesions [20,21]. However, the present study shows good diagnostic performance of attenuation drop for predicting MB compression. The main reason for this discrepancy may be explained by different analysis methods used in the current and previous studies. Percentage attenuation drop only measures the intraluminal attenuation change of two closely located segments and differs from TAG, which evaluates the intraluminal attenuation change of the whole coronary artery. Therefore, luminal size does not have a large impact on the analysis results. The clinical implication of this novel parameter lies in its ability to rule out significant dynamic compression of MB using only diastolic phase images. Prospective ECG-gated CTA acquisition might potentially benefit from this promising application with the possibility to select proper candidates for further functional tests with lower radiation dose.

The major limitation of this study is its retrospective design and lack of functional tests for correlation. Since the majority of the study cohort did not undergo myocardial perfusion imaging, we were not able to determine whether this percentage attenuation drop was associated with hemodynamic status in MB cases. In addition, ICA was not available in most patients to confirm the diagnosis of significant dynamic compression.

In conclusions, the percentage attenuation drop of MB segment significantly correlated with the extent of dynamic compression of MB. Percentage attenuation drop $\geq 15\%$ (the best cutoff value) has high diagnostic accuracy (73.3%, 99/135) to identify significant dynamic compression of MB.

Conflicts of Interest

The authors declare that they have no conflict of interest.

Acknowledgments

This study is supported by the National Natural Science Foundation of China (Grant No.: 81671678) and Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (Grant No.: 20161428).

REFERENCES

- Geiringer E. The mural coronary. *Am Heart J* 1951;41:359-368.
- Möhlenkamp S, Hort W, Ge J, Erbel R. Update on myocardial bridging. *Circulation* 2002;106:2616-2622.
- Ishii T, Asuwa N, Masuda S, Ishikawa Y. The effects of a myocardial bridge on coronary atherosclerosis and ischaemia. *J Pathol* 1998;185:4-9.
- Corban MT, Hung OY, Eshtehardi P, Rasoul-Arzrumly E, McDaniel M, Mekonnen G, et al. Myocardial bridging: contemporary understanding of pathophysiology with implications for diagnostic and therapeutic strategies. *J Am Coll Cardiol* 2014;63:2346-2355.
- Berry JF, von Mering GO, Schmalfuss C, Hill JA, Kerensky RA. Systolic compression of the left anterior descending coronary artery: a case series, review of the literature, and therapeutic options including stenting. *Catheter Cardiovasc Interv* 2002;56:58-63.
- Gowda RM, Khan IA, Ansari AW, Cohen RA. Acute ST segment elevation myocardial infarction from myocardial bridging of left anterior descending coronary artery. *Int J Cardiol* 2003;90:117-118.
- Tio RA, Ebels T. Ventricular septal rupture caused by myocardial bridging. *Ann Thorac Surg* 2001;72:1369-1370.
- Ural E, Bildirici U, Celikyurt U, Kilic T, Sahin T, Acar E, et al. Long-term prognosis of non-interventionally followed patients with isolated myocardial bridge and severe systolic compression of the left anterior descending coronary artery. *Clin Cardiol* 2009;32:454-457.
- Kodama K, Morioka N, Hara Y, Shigematsu Y, Hamada M, Hiwada K. Coronary vasospasm at the site of myocardial bridge report of two cases. *Angiology* 1998;49:659-663.
- Tio RA, Van Gelder IC, Boonstra PW, Crijns HJ. Myocardial bridging in a survivor of sudden cardiac near-death: role of intracoronary doppler flow measurements and angiography during dobutamine stress in the clinical evaluation. *Heart* 1997;77:280-282.
- Morales AR, Romanelli R, Boucek RJ. The mural left anterior descending coronary artery, strenuous exercise and sudden death. *Circulation* 1980;62:230-237.
- Leschka S, Koepfli P, Husmann L, Plass A, Vachenaue R, Gaemperli O, et al. Myocardial bridging: depiction rate and morphology at CT coronary angiography--comparison with conventional coronary angiography. *Radiology* 2008;246:754-762.
- Kim PJ, Hur G, Kim SY, Namgung J, Hong SW, Kim YH, et al. Frequency of myocardial bridges and dynamic compression of epicardial coronary arteries: a comparison between computed tomography and invasive coronary angiography. *Circulation* 2009;119:1408-1416.
- Kawawa Y, Ishikawa Y, Gomi T, Nagamoto M, Terada H, Ishii T, et al. Detection of myocardial bridge and evaluation of its anatomical properties by coronary multislice spiral computed tomography. *Eur J Radiol* 2007;61:130-138.
- Zeina AR, Odeh M, Blinder J, Rosenschein U, Barmer E. Myocardial bridge: evaluation on MDCT. *AJR Am J Roentgenol* 2007;188:1069-1073.
- Jodocy D, Aglan I, Friedrich G, Mallouhi A, Pachinger O, Jaschke W, et al. Left anterior descending coronary artery myocardial bridging by multislice computed tomography: correlation with clinical findings. *Eur J Radiol* 2010;73:89-95.
- Bourassa MG, Butnaru A, Lespérance J, Tardif JC. Symptomatic myocardial bridges: overview of ischemic mechanisms and current diagnostic and treatment strategies. *J Am Coll Cardiol* 2003;41:351-359.
- Schwarz ER, Gupta R, Haager PK, vom Dahl J, Klues HG, Minartz J, et al. Myocardial bridging in absence of coronary artery disease: proposal of a new classification based on clinical-angiographic data and long-term follow-up. *Cardiology* 2009;112:13-21.
- Schwarz ER, Klues HG, vom Dahl J, Klein I, Krebs W, Hanrath P. Functional, angiographic and intracoronary doppler flow characteristics in symptomatic patients with myocardial bridging: effect of short-term intravenous beta-blocker medication. *J Am Coll Cardiol* 1996;27:1637-1645.
- Park EA, Lee W, Park SJ, Kim YK, Hwang HY. Influence of coronary artery diameter on intracoronary transluminal attenuation gradient during CT angiography. *JACC Cardiovasc Imaging* 2016;9:1074-1083.
- Bom MJ, Driessen RS, Stuijzand WJ, Raijmakers PG, Van Kuijk CC, Lammertsma AA, et al. Diagnostic value of transluminal attenuation gradient for the presence of ischemia as defined by fractional flow reserve and quantitative positron emission tomography. *JACC Cardiovasc Imaging*. 2017 Dec 8 [Epub]. <https://doi.org/10.1016/j.jcmg.2017.10.009>.