The transluminal attenuation gradient does not add diagnostic accuracy to coronary computed tomography

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The transluminal attenuation gradient does not add diagnostic accuracy to coronary computed tomography Abstract

Background: A method for improving the accuracy of Coronary CT angiography (CCTA) is highly sought after as it would help to avoid unnecessary invasive coronary angiographies. Measurement of the transluminal attenuation gradient (TAG) has been proposed as an alternative to other existing methods i.e. CT perfusion and CT fractional flow reserve.

Purpose: To evaluate the incremental value of three types of transluminal attenuation gradients (TAG) in high pitch spiral CCTA with invasive fractional flow reserve (FFR) measurements as reference.

Material and Methods: TAG was measured using two semiautomatic and one manual method. An ROC analysis was made to determine the usefulness of TAG alone as well as TAG combined with CCTA for detection of significant coronary artery stenoses defined by an invasive FFR value ≤0.80.

Results: A total of 51 coronary vessels in 37 patients were included in this retrospective study. Hemodynamically significant stenoses were found in 13 vessels according to FFR. The ROC analysis TAG alone resulted in AUCs of 0.530 and 0.520 for the semi-automatic TAG and 0.557 for the manual TAG. TAG and CCTA combined resulted in AUCs of 0.567, 0.562 for semi-automatic TAG and 0.569 for the manual TAG.

Conclusion: The results from our study showed no incremental value of TAG measured in single heartbeat CCTA in determining the severity of coronary artery stenosis degrees.

Keywords

CT-Angiography, Coronary arteries, Transluminal attenuation gradient, Stenosis evaluation

Introduction

The diagnostic accuracy for coronary angiography is high and it is considered to be the reference standard for stenosis degree evaluation when the fractional flow reserve (FFR) is

measured (1,2). Due to its invasive nature it is however associated with a certain risk for complications (3) as well as being a relatively costly procedure (4). Coronary CT angiography (CCTA) examinations have emerged as a non-invasive alternative primarily for patients with an intermediate or low pre-test likelihood for cardiovascular disease. According to the clinical practice guidelines (5) published in 2019 by the European society of cardiology CCTA is to be used as the initial test to diagnose chronic coronary artery disease (CAD) in symptomatic patients when CAD cannot be ruled out by clinical assessment. Thus replacing exercise stress ECG in the management of these patients (5). Several studies have shown very good sensitivity for CCTA in detecting coronary artery stenoses (4,6). The specificity on the other hand has shown to be lower and more varying. Evaluations of calcified plaques are especially problematic as calcifications cause so called blooming artefacts that blur the edges of the plaque (4). This leads to overestimations of the stenosis degree and therefore also to unnecessary coronary angiographies (4,6). Methods that add functional information to the CCTA such as stress myocardial CT perfusion (CTP) and fractional flow reserve CT (CT-FFR) have been shown to improve the specificity (7,8). CTP does however require additional imaging and CT-FFR is still only available as an off-site analysis (9).

Another method that has been proposed for improvement of the accuracy of CCTA is measurement of the transluminal attenuation gradient (TAG). The theory behind TAG is that the contrast attenuation throughout the coronaries reflects the blood flow. By simply measuring the attenuation along the centreline of the vessel at several points a linear regression coefficient can be calculated. A stenosis will reduce the blood flow and contrast delivery thereby causing an increase of the regression coefficient (10–12). TAG can be measured manually using the same software used for standard CCTA evaluations or by using specialized semi- or fully automated software. Studies made so far have shown contradictory results (11,13–19). This is possibly due to the lack of an established standard for TAG regarding the CCTA scan protocol, the contrast injection protocol or the image reconstruction parameters. Using 320 slice detectors seems to give a slightly more reliable TAG result (15–17,20–22) likely thanks to a better temporal uniformity of the contrast phase as the entire heart is imaged during a single heartbeat. Another way to achieve single-beat CCTA acquisitions is to use a high pitch spiral technique (23). This type of scan is available in dual source CT systems and renders a scan speed fast enough to capture images of the entire heart during diastole in patients with a heart rate below 65-70 bpm (24). TAG analysis has not previously been evaluated in high pitch spiral CCTA however.

The aim of this study was to evaluate manual and semi-automatic TAG in high pitch spiral CCTA examinations for coronary stenosis evaluations with invasive FFR measurements as reference.

Material and Methods

Ethical approval for this retrospective cross-sectional study was granted by the regional ethical review board as an amendment (Dnr M6-09) to a previously approved application (Dnr 2013/278-32). All CCTA examinations had been performed at ………. University hospital and were entered into the national SWEDEHEART registry. The included examinations were anonymized and provided with a study ID before any of the evaluations took place. The need for informed consent was waived according to Swedish legislation regarding national quality registries and due to the retrospective nature of the study.

Patients

CCTA examinations performed between August 2009 and March 2017 were eligible for inclusion in this analysis. Consecutive sampling was used to include high pitch spiral examinations that had been followed up with coronary angiography and FFR within 90 days. Only one examination per patient was included. CCTAs of patients with congenital heart disease and patients that had undergone a heart transplantation or bypass surgery were excluded.

All the CT image evaluations were made by a cardiac imaging radiographer (L.H.) with level 1 training for cardiac CT reading as defined by the society of cardiovascular CT (25) and 2 years' experience of cardiac CT research reading. The image quality of the CCTAs was assessed by the reader and graded on a 5 point scale; unassessable, poor, measurable, good, excellent. Examinations fulfilling the three highest levels were included in the study. Only stenoses located in the right coronary artery (RCA), left anterior descending artery (LAD) or the circumflex (Cx) artery were assessed (Fig. 1.).

CCTA image acquisition and evaluation

Three different CT scanners were used for CCTA examinations throughout the inclusion period: Two 2x128-channel dual source scanners (SOMATOM Definition Flash and Definition Flash with Stellar detector, Siemens Healthineers, Forchheim, Germany 2009-2012 and 2012-2014 respectively) and one 2x192-channel dual source scanner (Somatom Force, Siemens, 2014-). A prospectively ECG-gated high-pitch spiral protocol was used to acquire images of the entire heart during the diastolic phase in one heartbeat. Scan parameters used were; qRef. mAs 324, ref. kV 100kV, pitch 3.4, rotation time 0.28 s (Flash) or 0.25 s (Force), temporal resolution 78 ms (Flash) or 66 ms (Force). Imaging of the heart started at 60 % of the heart cycle and continued until about 90 % depending on the scan length. A stable heart rate under 60 bpm was needed for this type of scan as there is a risk that higher more unstable heart rates will cause motion artefacts. Betablockers (up to 10 mg Metoprolol) were administered to lower the pulse in patients with a heart rate > 65 bpm. Nitroglycerine (up to 1.2 mg) was administered to optimize the contrast filling. A test bolus of 10 ml iodine contrast (Iopromide, Ultravist 370 mgI/ml, Schering, Berlin, Germany), followed by 50 ml saline solution was injected to calculate the optimal scan delay. The contrast dose was 335 mgI/kg (maximum weight 77 kg) and the injection time was 11.5 s.

The results for the CCTA examinations were retrieved from the clinical radiology reports. All evaluations had been made by radiologists specialized in CCTA image analysis. The reports did not contain quantitative evaluations of the stenosis degree instead the severity was reported as non-significant, possibly significant or significant.

Coronary angiography and FFR

Coronary angiographies were performed within 90 days after the CCTA for all included examinations. The FFR measurement was done using a dedicated guidewire (PressureWire Certus, St. Jude Medical Systems, Uppsala, Sweden) that was inserted in the vessel and advanced beyond the stenosis. Adenosine (140 µg/kg/min) was administered before the measurement to increase the blood flow. FFR was calculated as the mean pressure distally of the stenosis divided by the blood pressure in the aorta. An FFR of ≤0.80 was considered hemodynamically significant.

TAG

All included examinations were anonymized and provided with a study ID before any of the evaluations took place. TAG measurements were made by the same reader (L.H.) who was blinded to the previous results from the CCTA, coronary angiography and FFR measurement. A training set of 10 CCTA examinations was evaluated before starting the evaluations of the study examinations. Results from the training set were not included in the study results.

The semi-automatic CT software (QAngio CT Research edition 2.0.5, Medis medical imaging systems, the Netherlands) provided measurements of the attenuation at 0.5 mm intervals from the ostium until the cross-sectional area tapered below 2 mm^2. It automatically segmented the centerline as well as the outlines of the vessel wall. These segmentations were corrected by the reader when needed. Two types of TAG were derived by the software, one that included the attenuation of the entire ostium (TAG) at each measurement site and one only including the attenuation in a 3x3 pixel patch around the centerline (TAG_p).

The manual TAG (TAG_m) evaluation was performed using a server based work station (Syngo.via, Siemens Healthineers) and the applied method has been described in previous articles (16,17). A centreline was determined for each included vessel by the software and manually corrected if necessary. Regions of interest (ROIs) were positioned in cross-sectional images perpendicular to the centreline. The 1 mm^2 ROIs were placed at a 5 mm distance from each other from the ostium until a vessel cross-sectional area < 2 mm^2 was reached.

The TAG value was defined as the linear regression line from the ostium until the end of the included part of the vessel. The final TAG was defined as HU/10 mm as in previous articles (11,16,19).

Statistical analysis

Statistical analyses were performed using IBM SPSS version 26.0.0.0 (IBM SPSS statistics, Armonk, New York). Continuous variables with normal distribution are presented as mean ± SD and variables with non-normal distribution are presented as median and interquartile range. Categorical variables are presented as frequencies and percentages. Receiver operating characteristics (ROC) curves were used to demonstrate the value of TAG measurements alone for determining the significance of the stenosis degree according to the FFR results. The combined value of CCTA and TAG was checked by first using logistic regression to calculate

the probability of TAG to correspond to the estimated stenosis significance level for each vessel. This probability was then evaluated against the FFR result using ROC analysis.

Results

Study population

The results are based on the inclusion of 37 patients (21 men, 16 women 50 to 84 years of age) and a total of 51 vessels (32 LAD, 8 Cx, 11 RCA), that were all considered to be of measurable, good or excellent image quality. The mean time between the CCTA and the coronary angiography was 52 days. Included patients had a mean age of 61.9±8.0 years, mean body mass index of 27±4.1. The mean heart rate during the CCTA was 57±17 and the mean radiation dose from the CCTA and invasive coronary angiography was 1.44 mSv and 6.6 mSv respectively. Diabetes mellitus was found in three patients, dyslipidemia in 17 patients and hypertension in 20 patients. Out of the 37 patients four were smokers and 17 were ex-smokers. Patient characteristics are presented in Table 1.

Coronary angiography and FFR

Hemodynamically significant stenoses according to the FFR measurements were detected in 13 (25.5 %) vessels located in 13 (35.1 %) patients.

Transluminal attenuation gradient and CCTA

There were slight mean differences between the TAG, TAG_p and TAG_m values for vessels with FFR measurements below and above 0.8. These differences were however not statistically significant (Table 2). The ROC analysis of the TAG measurements alone resulted in AUCs of 0.530 (CI 0.357-0.703), 0.520 (CI 0.341-0.699) and 0.557 (CI 0.385-0.728) for TAG, TAG_p and TAG_m respectively (Fig. 2). According to the radiology reports 11 (22 %) vessels contained non-significant stenoses, 37 (72 %) possibly significant stenoses and 3 (6 %) significant. The probability values from the logistic regression analysis between TAG and CCTA resulted in ROC curves with AUCs of 0.567 (CI 0.395-0.738), 0.562 (CI 0.389 -0.734) and 0.569 (CI 0.398 -0.739) for TAG, TAG_p and TAG_m respectively (Fig. 3).

Discussion

In this study neither TAG nor the combination of TAG and CCTA provided additional information in determining the significance of coronary artery stenoses. Improving the specificity of CCTAs can lead to more efficient use of hospital resources and save patients from possible complications associated with coronary angiography. CTP and CT-FFR both improve the specificity of CCTAs by adding functional information to the anatomical map provided by the CCTA (22). TAG would be an attractive alternative to CTP and CT-FFR as it is accessible on-site and does not require additional radiation exposure of the patient (11,13–19).

Results from previous TAG studies have been contradictory and difficult to compare as there is no established standard for TAG measurement. The use of different CT systems, scan techniques, reconstruction parameters and contrast injection protocols could probably explain this some degree (26,27). A recently published meta-analysis that included TAG evaluations with FFR as reference method showed no significant improvement of the CCTA accuracy by using TAG. It did show a slight improvement when only 320 slice studies were included but the difference was still non-significant (22). Further studies including single heartbeat examinations have been warranted to evaluate TAG (28).

We tested three types of TAG i.e. one manual, and two types of semi-automatic measurements. The manual method has resulted in encouraging AUC values of 0.85 and 0.89 in two previous 320 slice TAG studies (16,17) which was higher than results from semi- and fully-automatic 320 slice TAG studies (15,20,21). One advantage of manual measurements is the control of the ROI placement as it could help avoiding contamination from artefacts in the attenuation measurement. This cannot be avoided using the semi-automated software. Even though the segmentation of the vessel wall is checked and corrected, the lumen opacification will still be affected by e.g. blooming artefacts in areas of calcified plaques or other potential artefacts in the examination. The TAG_p evaluation might be able to avoid this to some degree by only including pixel values close to the centreline. Blooming artefacts are caused by the limited spatial resolution of the CT system and become especially prominent in CCTAs performed with a lower kV setting i.e. 70 or 80 kV (29). Both semi-automatic measurements had the advantage of including attenuation values at every 0.5 mm which could contribute to a more exact gradient. Such frequent measurements would of course not be possible to do manually as it would be far too time consuming.

TAG is based on the assumption that the contrast opacification corresponds to the blood-flow throughout the coronary artery. However it does not take into consideration physiological aspects that could influence the blood flow and mixing of the contrast, such as the stenosis location, the number of branches leaving the vessel or the vessel diameter. This is all accounted for in CT-FFR (30) which also seems to be a method unaffected by vessel wall calcifications (31). Something that probably contributes to the gradient seen in TAG measurements is the small vessel diameter of the coronaries. This is indicated by the seeming correlation between TAG and the transluminal diameter gradient (TDG) i.e. the diameter change along the vessel length (28). If the vessel diameter becomes too small for the spatial resolution of the CT system voxels adjacent to the vessel start to contribute to the vessel attenuation i.e. partial volume effect. As the coronaries are surrounded by low attenuating soft tissues such as fat the result is a lowered attenuation and a potential overestimation of the TAG (27,28,32).

There are some limitations to this study. First is the relatively low number of patients and included vessels. Only 25 % of the included vessels had a significant stenosis according to the FFR measurement. However there is lack of previous TAG studies in flash technique CCTA and FFR measurements as reference at the moment. The main reason for the small number of examinations available for this study is that the high pitch spiral technique is only suitable for patients with a low and stable pulse. Imaging of the entire heart needs to take place during diastole to minimize the risk for motion artefacts. Second is the lack of a quantitative stenosis assessment in the CCTA images. This makes it impossible to assess the sensitivity and specificity for CCTA alone in this study. It also affected the ROC analysis for the combination of CCTA and TAG and makes the AUCs for the CCTA and TAG combination and TAG alone more difficult to compare. The main reason no quantitative assessment has been performed is that such measurements usually are considered to be of little clinical importance due to errors caused by CCTA image resolution issues. Third is the retrospective nature of the study. The included examinations are performed on three different CT systems and even though they were all state of the art and the same scan technique was applied, there are differences between them. Most importantly improvements of the detector configuration for the second system compared to the first and then again for the third system compared to the two earlier. This probably led to a difference in spatial resolution for the included examinations. Different kV settings were also applied depending on the patient size. This

could have contributed to blooming artefacts becoming more prominent in examinations performed with lower kV and thus also to a higher degree of error in the HU measurements.

The main strength of the study is the comparison of three types of TAG in single beat CCTA examinations using the gold standard reference i.e. FFR.

In conclusion our study shows that TAG measurements from CCTA data collected during a single heartbeat do not provide information valuable to the CCTA evaluation. We believe that TAG, at least in the present form, should not be used as an alternative to CTP and CT-FFR.

Funding

References

1. Zhang D, Lv S, Song X, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention: a meta-analysis. Heart Br Card Soc. 2015;101:455–462.

2. De Bruyne B, Pijls NHJ, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med. 2012;367:991–1001.

3. Start - SWEDEHEART. Available at: http://www.ucr.uu.se/swedeheart/start-scaar (accessed 8th April 2015)

4. Datortomografi för misstänkt kranskärlssjukdom - SBU. Available at: http://www.sbu.se/sv/Publicerat/Alert/Datortomografi-for-misstankt-kranskarlssjukdom/ (accessed 8th April 2015)

5. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019;31:1-71

6. Persson AS. Skiktröntgen undersöker hjärtat på några sekunder. Läkartidningen. 2008;22:3043–3046.

7.   De Geer J, Sandstedt M, Björkholm A, et al. Software-based on-site estimation of fractional flow reserve using standard coronary CT angiography data. Acta Radiol Stockh Swed 1987. 2016;57:1186–1192.

8. Rajani R, Modi B, Ntalas I, et al. Non-invasive fractional flow reserve using computed tomographic angiography: where are we now and where are we going? Heart Br Card Soc. 2017;103:1216–1222.

9. Schoepf UJ, Gray HN, Tesche C. CT Angiography–derived Fractional Flow Reserve: The Global Game of Thrones. Radiol Cardiothorac Imaging. 2019;31: https://doi.org/10.1148/ryct.2019190197.

10. Koo HJ, Yang DH, Kim Y-H, et al. CT-based myocardial ischemia evaluation: quantitative angiography, transluminal attenuation gradient, myocardial perfusion, and CT-derived fractional flow reserve. Int J Cardiovasc Imaging. 2016;14;1-19.

11. Steigner ML, Mitsouras D, Whitmore AG, et al. Iodinated contrast opacification gradients in normal coronary arteries imaged with prospectively ECG-gated single heart beat 320-detector row computed tomography. Circ Cardiovasc Imaging. 2010;3:179–186.

12. Rybicki FJ, Otero HJ, Steigner ML, et al. Initial evaluation of coronary images from 320-detector row computed tomography. Int J Cardiovasc Imaging. 2008;24:535–546.

13. Zheng M, Wei M, Wen D, et al. Transluminal attenuation gradient in coronary computed tomography angiography for determining stenosis severity of calcified coronary artery: a primary study with dual-source CT. Eur Radiol. 2015;25:1219–1228.

14. Chatzizisis YS, George E, Cai T, et al. Accuracy and reproducibility of automated, standardized coronary transluminal attenuation gradient measurements. Int J Cardiovasc Imaging. 2014;30:1181–1189.

15. Ko BS, Wong DTL, Nørgaard BL, et al. Diagnostic Performance of Transluminal Attenuation Gradient and Noninvasive Fractional Flow Reserve Derived from 320-Detector Row CT Angiography to Diagnose Hemodynamically Significant Coronary Stenosis: An NXT Substudy. Radiology. 2016;279:75-83.

16. Wong DTL, Ko BS, Cameron JD, et al. Transluminal attenuation gradient in coronary computed tomography angiography is a novel noninvasive approach to the identification of functionally significant coronary artery stenosis: a comparison with fractional flow reserve. J Am Coll Cardiol. 2013;26:1271–1279.

17. Wong DTL, Ko BS, Cameron JD, et al. Comparison of diagnostic accuracy of combined assessment using adenosine stress computed tomography perfusion + computed tomography angiography with transluminal attenuation gradient + computed tomography angiography against invasive fractional flow reserve. J Am Coll Cardiol. 2014;13:1904–1912.

18. Choi J-H, Koo B-K, Yoon YE, et al. Diagnostic performance of intracoronary gradient-based methods by coronary computed tomography angiography for the evaluation of physiologically significant coronary artery stenoses: a validation study with fractional flow reserve. Eur Heart J - Cardiovasc Imaging. 2012;1:1001–1007.

19. Choi J-H, Min JK, Labounty TM, et al. Intracoronary transluminal attenuation gradient in coronary CT angiography for determining coronary artery stenosis. JACC Cardiovasc Imaging. 2011;4:1149–1157.

20. Nagata K, Tanaka R, Takagi H, et al. Improved diagnostic performance of transluminal attenuation gradient in combination with morphological evaluation of coronary artery stenosis using 320-row computed tomography. Jpn J Radiol. 2018;36:51–58.

21. Kato E, Fujimoto S, Takamura K, et al. Clinical significance of transluminal attenuation gradient in 320-row area detector coronary CT angiography. Heart Vessels. 2018;33:462–469.

22. Hamon M, Geindreau D, Guittet L, et al. Additional diagnostic value of new CT imaging techniques for the functional assessment of coronary artery disease: a meta-analysis. Eur Radiol. 2019;29:3044–3061.

23. Kim HJ, Kim SM, Choi J-H, et al. Influence of scan technique on intracoronary transluminal attenuation gradient in coronary CT angiography using 128-slice dual source CT: multi-beat versus one-beat scan. Int J Cardiovasc Imaging. 2017;33:937–946.

24. Bogaard K, van der Zant FM, Knol RJJ, et al. High-pitch prospective ECG-triggered helical coronary computed tomography angiography in clinical practice: image quality and radiation dose. Int J Cardiovasc Imaging. 2015;31:125–133.

25. Maroules CD, Cheezum MK, Joshi PH, et al. SCCT curriculum guidelines for general (level 1) cardiovascular CT training. J Cardiovasc Comput Tomogr. 2015;9:81–88.

26. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010;256:32–61.

27. Wang J, Fleischmann D. Improving Spatial Resolution at CT: Development, Benefits, and Pitfalls. Radiology. 2018;289:261–262.

28. Bom MJ, Driessen RS, Stuijfzand WJ, 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. 2019;12:323–333.

29. Mannelli L, Mitsumori LM, Ferguson M, et al. Changes in measured size of atherosclerotic plaque calcifications in dual-energy CT of ex vivo carotid endarterectomy specimens: effect of monochromatic keV image reconstructions. Eur Radiol. 2013;23:367–374.

30. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: scientific basis. J Am Coll Cardiol. 2013;61:2233–2241.

31. Tesche C, Otani K, De Cecco CN, et al. Influence of Coronary Calcium on Diagnostic Performance of Machine Learning CT-FFR: Results From MACHINE Registry. JACC Cardiovasc Imaging. 2019; https://doi.org/10.1016/j.jcmg.2019.06.027

32. Park E-A, Lee W, Park SJ, Kim YK, et al. Influence of Coronary Artery Diameter on Intracoronary Transluminal Attenuation Gradient During CT Angiography. JACC Cardiovasc Imaging. 2016;9:1074–1083.
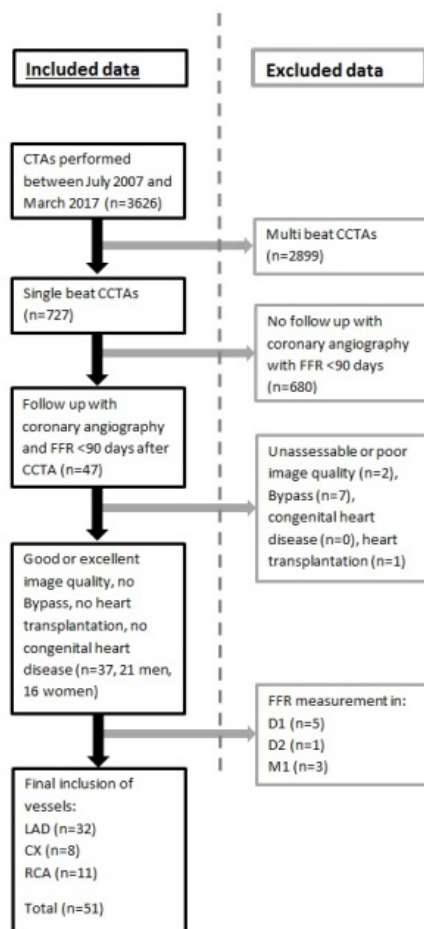
Fig. 1 Inclusion and exclusion of coronary CT angiography (CCTA) examinations based on follow up with coronary angiography and fractional flow reserve (FFR), image quality assessment and stenosis location. Stenoses in the left anterior descending (LAD), Circumflex (CX) and right coronary arteries were included while stenoses in diagonal (D1, D2) marginal branches (M1) were excluded.

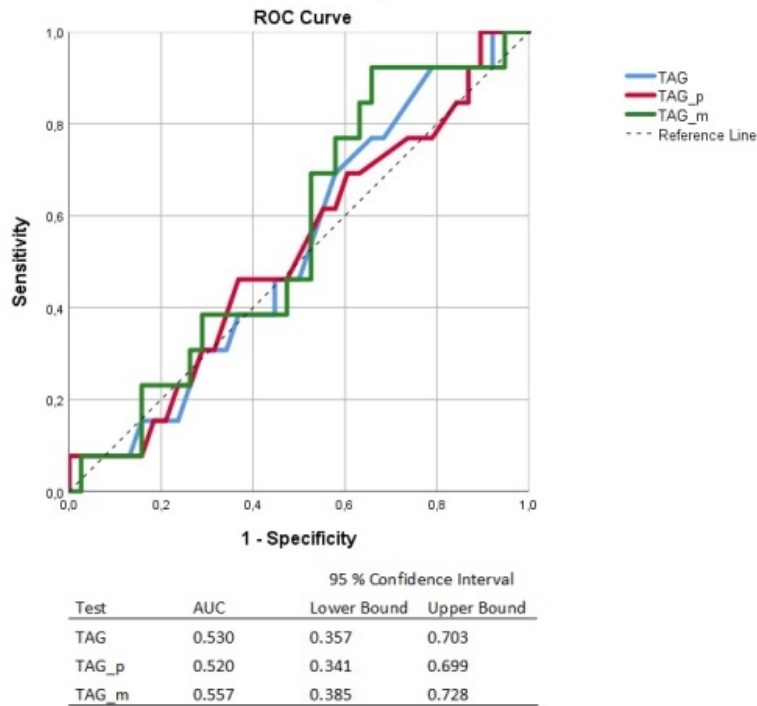| Test	AUC	95 % Confidence Interval	
		Lower Bound	Upper Bound
TAG	0.530	0.357	0.703
TAG_p	0.520	0.341	0.699
TAG_m	0.557	0.385	0.728

Fig. 2 Receiver operating characteristic curves for the diagnostic accuracy of semi-automatic TAG including attenuation measurements of the entire ostium (TAG), TAG in a 3x3 pixel patch (TAG_p) around the centerline and manually measured TAG (TAG_m) using fractional flow reserve (FFR) measurements ≤0.80 as reference.

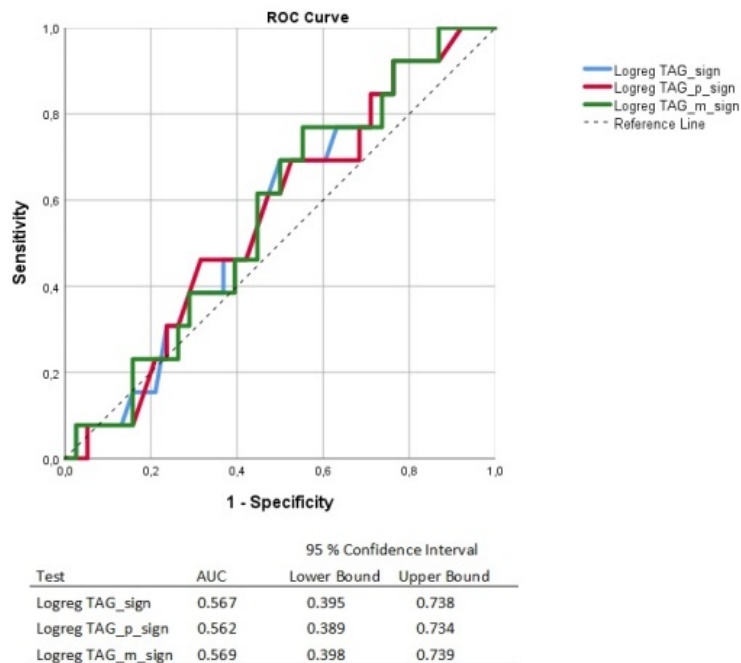| Test	AUC	95 % Confidence Interval	
		Lower Bound	Upper Bound
Logreg TAG_sign	0.567	0.395	0.738
Logreg TAG_p_sign	0.562	0.389	0.734
Logreg TAG_m_sign	0.569	0.398	0.739

Fig. 3 Receiver operating characteristic curves for the diagnostic accuracy of probability values derived by logistic regression between the coronary CT angiography (CCTA) assessment and semi-automatic TAG including attenuation measurements of the entire ostium (Logreg TAG_sign), TAG in a 3x3 pixel patch (Logreg TAG_p_sign) around the centerline and manually

measured TAG (Logreg TAG_m_sign) using fractional flow reserve (FFR) measurements ≤0.80 as reference.

Table 1 Patient characteristics and radiation dose

Patient characteristics		Range
Number of patients	37	
Male	21 (57 %)	
Age (years)	61.9±8.0	
heart rate	57±17	45-150
Body mass index	27±4.1	20-37
Time from CCTA to invasive angiography (days)	52±24	2-90
Radiation dose CCTA (mSv)	1.44	
Radiation Dose invasive angiography (mSv)	6.6	
Diabetes Mellitus	3 (8 %)	
Smokers/Ex-Smokers	4 (11 %)/17 (46 %)	
Dyslipidemia (%)	17 (46 %)	
Hypertension (%)	70 (54 %)	

Table 2 Transluminal attenuation gradients for vessels with FFR measurements below and above 0.8.

	Total	FFR >0.80	FFR ≤0.80	P Value (FFR groups)
All vessels	51	38	13	
TAG	-24.06 ±13.55	-23.83±13.56	-24.75±3.89	0.21
TAG_p	-23.13 ±14.28	-22.97±14.61	-23.58±13.84	0.13
TAG_m	-19.23 ± 11.39	-18.89±11.88	-20.2±10.20	0.35

Semi-automatic TAG including attenuation measurements of the entire ostium (TAG), TAG in a 3x3 pixel patch (TAG_p) around the centerline and manually measured TAG (TAG_m). The values presented are n or mean ± SD analysis on a per vessel basis stratified by Fractional Flow Reserve (FFR) results.