International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Diagnostic accuracy of ASLA score (a novel CT angiographic index) and aggregate plaque volume in the assessment of functional significance of coronary stenosis

Ravi Kiran Munnur [a,*], James D. Cameron [a], Liam M. McCormick [a], Peter J. Psaltis [b,c], Nitesh Nerlekar [a], Brian S.H. Ko [a], Ian T. Meredith [a], Sujith Seneviratne [a], Dennis T.L. Wong [a,b]

[a] Monash Cardiovascular Research Centre, Department of Medicine (Monash Medical Centre) Monash University and Monash Heart, Monash Health, 246 Clayton Road, Clayton, 3168, VIC, Australia
[b] South Australian Medical Research Institute (SAHMRI), Adelaide, Australia
[c] Discipline of Medicine, University of Adelaide, Adelaide, Australia

ARTICLE INFO

Article history:
Received 3 February 2018
Received in revised form 5 June 2018
Accepted 6 June 2018
Available online xxxx

Keywords:
ASLA score
Percent aggregate plaque volume
Computed Tomography Coronary Angiography
Coronary artery disease
Fractional flow reserve

ABSTRACT

Background: Visual assessment of diameter-stenosis on Computed Tomography Coronary Angiography (CTCA) lacks specificity to determine functional significance of coronary artery stenosis. Percent-aggregate plaque volume (%APV) and ASLA score, which incorporates **A**rea of **S**tenosis, **L**esion length, and area of myocardium subtended estimated by **A**PPROACH score (Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease) have been described to predict lesion specific ischaemia in focal lesions with intermediate stenosis.

Methods and results: Included were 81 patients (mean age 64.7 ± 9 years, 62% male; 94 vessels) who underwent 320- detector-row CTCA, invasive coronary angiography and fractional-flow-reserve (FFR). We examined vessels with wide range of diameter stenosis (mid to severe) and with multiple lesions. Invasive FFR of ≤0.8 was considered functionally significant.

The first 54 patients (62 vessels) formed the derivation cohort. ASLA score was the best predictor of FFR ≤ 0.8 (AUC 0.83, $p < 0.001$) compared to %APV (0.72), CT >50% (0.76), APPROACH score (0.79), area-stenosis (0.73), diameter-stenosis (0.74), minimum-luminal-diameter (0.74), minimal-luminal-area (0.72), and lesion-length (0.67). ASLA score and not %APV, provided incremental predictive value when added to CT > 50 [(NRI 0.71, $p = 0.005$) vs. (NRI 0.01, $p = 0.96$)].

In the validation cohort of 27 patients (32 vessels), the ASLA score (AUC 0.85) was again a better predictor of FFR ≤ 0.8 compared to %APV (0.71), CT > 50% (0.66) and other CT indices. The AUC of ASLA score was superior to CTCA>50% ($p = 0.001$).

Conclusion: ASLA score is a novel predictor of functional significance of coronary stenosis and adds incremental predictive value to CT > 50 but %APV did not.

1. Introduction

Computed Tomography Coronary Angiography (CTCA) is an established non-invasive test to detect coronary stenosis in individuals with low to intermediate risk of coronary artery disease (CAD) [1, 2]. However, CTCA is limited by low specificity to predict lesion specific ischaemia and visual or quantitative assessments of coronary stenosis do not correlate well to fractional flow reserve (FFR) [3]. In addition, even the presence of obstructive disease on CTCA had poor predictive value of ischaemia on myocardial perfusion tests [4–6]. Studies have shown that besides diameter stenosis, predictors of fractional flow reserve (FFR) ≤ 0.8 are area stenosis, lesion length and ischaemic burden [7–9]. In addition, for intermediate stenosis, lesions in proximal LAD with larger myocardial supply and ischaemic burden had more significant FFR values compared to distal LAD, left circumflex artery and right coronary artery [10]. Based on these observations, the ASLA (Area Stenosis Lesion length and APPROACH score) score has been described. It was demonstrated to predict significant FFR and provide incremental predictive value over individual indexes alone [11].

Abbreviations: CTCA, Computed Tomography Coronary Angiography; ICA, invasive coronary angiography; CAD, coronary artery disease; APV, aggregate plaque volume; ASLA, area stenosis, lesion length, area of myocardium subtended by APPROACH score; IVUS, intravascular ultrasound; FFR, fractional flow reserve; APPROACH, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease; SM, supplementary material; HU, Hounsfield unit; MLA, minimum luminal area; MLD, minimum luminal diameter; QCT, quantitative computed tomography; AUC, area under curve; NRI, net reclassification index.

* Corresponding author at: Monash Medical Centre, Monash Cardiovascular Research Centre, VIC, Australia.
E-mail address: kiran.munnur@gmail.com (R.K. Munnur).

https://doi.org/10.1016/j.ijcard.2018.06.022
0167-5273/

It incorporates lesion length, area of stenosis and the area of myocardium subtended by coronary stenosis estimated by APPROACH score (Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease).

In addition to the identification of luminal stenosis, plaque quantification can also be derived from CTCA [12]. Nakazato et al. demonstrated that percent aggregate plaque volume (%APV) was the best predictor of FFR significant lesions amongst various CTCA indexes and it was shown to provide incremental diagnostic value when added to individual CTCA indexes [13]. To date, diagnostic accuracy of the ASLA score and percent APV have been evaluated only in vessels with focal lesions with intermediate diameter stenosis severity. In this study, we assessed and compared the diagnostic accuracy of ASLA score and percent APV in vessels with wide range of stenosis severity and in vessels with multiple stenoses.

2. Methods

We included consecutive patients with suspected coronary artery disease who underwent clinically indicated 320 detector–row CTCA and ICA with FFR within a three month period between December 2013 and January 2015. FFR assessment was performed in at least one lesion of mild (>30%) severity as visually assessed on CTCA. Our institutional Human Research Ethics Committee approved the study. Excluded were patients with >3 months duration between CTCA an FFR, poor quality images, prior coronary artery bypass grafting, left ventricular dysfunction, acute coronary syndrome and vessels with more than one severe lesion, severe calcification, diffuse disease, severe stenosis in the distal segment, intra coronary stents and small vessel diameter (<2 mm).

2.1. CT coronary angiography

Patients underwent cardiac CT assessment using a 320-row detector CT scanner (Aquilion One Vision; Toshiba Medical Systems Corp., Tokyo, Japan). All patients received sublingual nitroglycerine, and additional beta-blockers were administered to achieve a pre-scan heart rate of <60 beats/min in accordance with Society of Cardiovascular Computed Tomography guidelines [14].

A bolus of 55 mL of 100% iohexol 56.6 g/75 mL (Omnip-aque 350; GE Healthcare, Princeton, NJ) was injected into an antecubital vein at a low rate of 5 mL/s, followed by 20 mL of a 30:70 mixture of contrast material and saline, followed by 30 mL of saline. Scanning parameters were as follows: detector collimation: 320 × 0.5 mm; tube current: 300–500 mA (depending on body mass index), tube voltage: 120 kV; gantry rotation time: 350 ms; and temporal resolution: 175 ms. Prospective electrocardiographic gating was used, covering phases 70%– 80% of the R-R interval. Scanning was completed with a single R-R interval utilizing a 180° segment if heart rate was <65 beats per minute or slower and data segments from two consecutive beats were used for multi-segment reconstruction with an improved temporal resolution of 87 ms in patients with a heart rate >65 beats per minute,

2.2. Analysis of CT coronary angiograms

Data was transferred to an external workstation (Vitrea 6, version 6.0; Vital Images, Minnetonka, Minnesota) for further analysis. Two experienced cardiologists (KM & DW) who were blinded to the results of coronary angiography and FFR measurements performed the analysis independently. Plaque quantification was performed using a dedicated software tool (Sure Plaque, Vitrea 6, version 3.0; Vital Images and Toshiba Medical Systems). Further manual adjustments were performed for the lumen and the outer vessel wall using dedicated window settings [230 W and 83 L if the luminal Hounsfield unit (HU) was <500; and 300 W and 150 L if the luminal HU was >500] [15]. If necessary, additional window setting of 740 W/220 L and 1400 W/400 L were used in the presence of non-calcified and calcified plaque respectively, to assess outer vessel wall [16] (Fig. 1) (SM Fig. 4).

Vessels were categorised based on visual diameter stenosis of >50% (CT > 50) and quantitative computed tomography (QCT) stenosis >70%. APPROACH score was used to evaluate the proportion of the myocardium perfused by each artery as previously described [17, 18] (SM Table 3). The modified score considers the location of the lesion (proximal, middle, or distal) and the dominance and size of the secondary branches and provides an estimate of the percentage of supplied myocardium beyond the considered coronary lesion. For the assessment of ASLA score, each lesion was assigned individual score based on lesion length, area stenosis and APPROACH score as previously described [11]. ASLA score was derived after addition of individual scores for a possible total of 18 points (Table 1). In vessels with multiple stenoses, the most significant lesion was analysed for minimal luminal area (MLA), minimal luminal diameter (MLD), lesion length and ASLA score (SM Fig. 3).

For the assessment of percent APV, ostium to the distal edge of the lesion in vessels with single lesion and from the ostium to the distal edge of the distal lesion in vessels with multiple lesions was considered. As a first step, plaque area defined as the area between the outer contour of the vessel (vessel area) and the lumen at each slice (0.5 mm) was determined. Secondly, aggregate plaque volume was obtained by summation of all plaque areas. Thirdly, total vessel volume was derived from the summation of all vessel areas. Percent aggregate plaque volume was calculated as aggregate plaque volume divided by total vessel volume and reported as percentage [13].

2.3. Invasive coronary angiography and FFR measurement

Invasive coronary angiography was performed as per standard catheterisation procedure in accordance with the American College of Cardiology guidelines for coronary angiography [19]. FFR was measured using pressure sensor tipped guide wire (Pressure wire Certus; St Jude Medical, St Paul, Minn) as previously described. Intracoronary glyceryl trinitrate (100 μg) was injected to minimise vasospasm. Intravenous adenosine was administered at 140 μg/kg/min through an intravenous line in the antecubital fossa. At steady state hyperaemia, FFR was assessed by using the Radi Analyser Xpress (St Jude Medical) and was calculated by dividing the pressure obtained distal to the stenosis to the mean aortic pressure measured through the guide catheter. An FFR of 0.8 or less was considered to indicate lesion-specific ischaemia [20].

2.4. Statistical analysis

Continuous variables are expressed as mean ± standard deviations or with 95% confidence interval. Categorical variables are expressed as percentages. Continuous and categorical variables were compared using *t*-test, Mann-Whitney or chi-square as appropriate. Correlations between coronary CTA parameters and FFR were assessed by calculating Pearsons correlation coefficient. Inter-observer variability was assessed by using the intra-class coefficient and Bland Altman test. For Univariate binary logistic regression analysis, standardised odds ratio coefficients were added to enable direct comparison of predictors. Any cut off value of 0.25 on univariate analysis are usually included in the multivariate analysis and we chose covariates with $p < 0.2$ on univariate analysis to be included in the multivariate analysis by using the "enter" approach. For the multivariate logistic regression analysis, odds ratios were reported.

To examine discrimination, area under the receiver operating characteristic curves (AUC) were calculated and compared for the different CTCA parameters using De Long method [21]. We determined the net reclassification improvement of ASLA score and percent APV over CT > 50 to predict FFR ≤ 0.8. To determine intra-observer and inter-observer variability for calculation of percent APV and ASLA score, eighteen random subjects were selected (eight patients with FFR ≤ 0.8). A p value of <0.05 was considered statistically significant. Statistical analysis was performed with SPSS 18 (SPSS, Chicago, Ill).

3. Results

3.1. Patient characteristics

There were 145 patients who underwent CT and FFR assessment in our institution during the study period. All the patients in the study had CTCA initially for assessment of chest pain and the treating physician decided on the need for further investigations. Patients were excluded from the study for the following reasons: presence of minimal stenosis <30% (n = 16), poor image quality (n = 7), vessel diameter <2 mm (n = 14), excessive calcification (n = 17) and multiple severe tandem lesions (n = 10). The remaining 81 patients (mean age 64.7 ± 9 years, 62% male) with 94 vessels were included for analysis. The time interval between CTCA and FFR was less than three months. Of the 94 vessels (56 - LAD, 16 - LCx and 22 - RCA) included in the study, 42 vessels were FFR significant, 41 vessels had single lesion and 63 vessels had multiple lesions. There were 29 vessels with non-calcified plaque and remaining vessels had calcified or partially calcified plaque. Participants in the study did not undergo revascularisation between CTCA acquisition and FFR measurement and there were no events during this period. Patient characteristics are shown in Table 2.

The first 62 vessels were analysed for the assessment of diagnostic accuracy of ASLA score, %APV and various CT indices and formed the derivation cohort. The subsequent 32 vessels formed the validation cohort where the results were tested again.

4. Derivation cohort (54 patients and 62 vessels)

4.1. Relationship between CTCA parameters and significant FFR

There were 39 vessels (61%) with CT > 50 stenosis. On per vessel analysis, the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of CT > 50 for predicting significant FFR were 95%, 59%, 90% and 68% respectively. There were 22 vessels

Please cite this article as: R.K. Munnur, et al., Diagnostic accuracy of ASLA score (a novel CT angiographic index) and aggregate plaque volume in the assessment of functional significance of coronary stenosis, Int J Cardiol (2017), https://doi.org/10.1016/j.ijcard.2018.06.022