Original Article

Calculation of Coronary Angiographic Total Blush in Patients with Coronary Artery Disease and its Prognostic Implication

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Abstract

Background: Myocardial perfusion grade (MPG) is an accepted method of evaluating myocardial perfusion. However, it does not take into the account, the extent of the perfusion. We hypothesized that myocardial blush area times MPG (total blush) would be more accurate than simple MPG, and yield better prognostic information.
Methods: About 34 patients were recruited after they had consented to both coronary angiography (CAG) and single photon emission computed tomography (SPECT), and divided into two groups. A special dedicated computer was employed to calculate the total blush. The CAG was performed as a conventional way. Scintigraphic technetium 99m methoxyisobutyl-isonitrile rest and stress images were evaluated quantitatively. The comparison was made between stenosis versus chronic total occlusion (CTO), MPG 1, 2 versus MPG 3, percutaneous intervention (PCI) successful versus failure. A correlation was made between ejection fraction (EF) and myocardial perfusion by MPG, total blush, SPECT, and syntax score.
Results: The perfusion indices of total blush, summed difference score (SDS) and syntax score were insignificant between the two groups ($P > 0.05$). However, the left ventricular end diastolic volume was significantly larger in CTO ($P < 0.05$). The patients with stenosis had better MPG than with CTO ($P < 0.05$). The increased MPG was associated with increased total blush, higher syntax score, and EF ($P < 0.05$). Successful PCI resulted in better perfusion indicated by increased total blush, and MPG ($P < 0.05$) but successful PCI did not change syntax score, EF and SDS significantly. Multivariate linear analysis with EF as the dependent factor and syntax score, SDS, total blush, blush area, and MPG as the independent factors showed a significantly higher degree of correlation ($R = 0.87$, $P < 0.05$).
Conclusion: After PCI the total blush and EF improved significantly indicating its potential application in the future.

Key words: Coronary Heart Disease; Ejection Fraction; Myocardial Perfusion; Percutaneous Coronary Intervention; Single Photon Emission Computed Tomography; Syntax Score

Introduction

The myocardial perfusion grade (MPG) is the measurement of coronary myocardial perfusion.[1] It primarily aims to quantify the increase in gray value over time.[2] The darker the myocardium, the better the perfusion is. However, the blush grade does not take into account the area of the blush. It would be better if both the blush grade, and area of blush can be calculated. Vogelzang *et al*. have developed a computer program that allows the calculation of the Quantitative Blush Evaluator.[3] This program loads coronary angiograms in standard DICOM format. The operator selects the angiogram to use for assessment. On this angiogram, the operator indicates a polygonal shape that contains the distal area. When the operator has drawn the polygonal area, the program calculates the area in mm^2. The program is unavailable in China. The Crealife Company is specialized in cardiac imaging workstation. Yang *et al*. used the video densitometry to study the grayscale changes with time after contrast injection into the coronary artery.[4] The darker the myocardium, the higher the grayscale is. However, the variation of grayscale is too big to be of significant value according to our own experience. The computer workstation by Crealife provides the application of blush area calculation.

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The area of blush can be calculated by hand drawing the polygonal shape. The blush area times the degree of MPG is the total blush in our study. Theoretically, the better the perfusion, the better the left ventricular function is.[5] We, therefore, correlated the ejection fraction (EF) with syntax score, summed difference score (SDS), total blush, blush area, and MPG to see if better perfusion can also translate into better left ventricular function or better long term prognosis.

Methods

Patient selection

The patients with coronary artery disease (CAD) in People's Liberation Army General Hospital were consecutively recruited from March 2008 to August 2011 between the ages of 20–80 years. Both genders were included. The sample size included 34 patients. The inclusion criteria were: Both coronary angiography (CAG) and single photon emission computed tomography (SPECT) were performed, and data were collected. The patients were consented to undergo percutaneous intervention (PCI). The patients were divided into 3 groups, stenosis versus chronic total occlusion (CTO), MPG 1, 2 versus MPG 3, successful versus unsuccessful recanalization. The exclusion criteria were as follows: Previous coronary artery bypass graft (CABG); severe illness such as severe heart failure, respiratory disease, terminal cancer; pregnancy; renal function of chronic kidney disease 3 or more; allergy to iodine contrast. The relevant ethics committee of our hospital approved the protocol, and informed consents were taken from the patients before enrolment into the study.[6]

Coronary angiography and total blush calculation

A special dedicated computer manufactured by Crealife Company (Crealife Medical Technology, Beijing, China) was employed to calculate the total blush.[4] The CAG was performed as a conventional way. When maximal density was reached, the frames were frozen. The program then asks to manually draw the contours of the blushed myocardium. The area in mm^2 of the most blushed was displayed. The visual estimate of MPG was recorded. The blush area time blush grade was the total blush.

Single photon emission computed tomography imaging

Scintigraphic technetium 99m methoxyisobutyl-isonitrile (401 Institute, Beijing, China) rest (before PCI) and stress (after PCI) images were evaluated quantitatively after SPECT imaging (Dual-probe SPECT/CT, GE Infinia Hawkeye 4, USA) that employs a 17-segment left ventricular model with a common five-point scoring system (0 = "normal perfusion;" 4 = "no perfusion").[7] The results were interpreted by two co-investigators blinded to clinical feature and laboratory test results. The summed stress scores (SSS) and summed rest scores (SRS) of all segments were determined. The SDS was calculated as the difference between the SSS and the SRS. An SDS ≥4 was defined as stress-induced ischemia and counted as pathological SPECT-myocardial perfusion imaging (MPI).

Treatment strategy

CAG was performed by the GE Innova 3100 angiography system (GE Healthcare, USA) through the femoral or radial artery according to the physician preference. Angiograms were read by two experienced investigators. Syntax score was calculated.[8,9] The decision regarding treatment strategy was made by noninvasive cardiologists.

Statistical analysis

Statistical analysis was performed with SPSS 19.0 (SPSS, Inc., Chicago, IL, USA). Continuous data representing normal distribution were expressed as mean ± standard deviation, and continuous data that did not pass the normality test were expressed as median (P_{25}, P_{75}). Categorical variables were expressed as frequencies or percentages. The *t*-test and Chi-square test were used to determine their significance. Multivariate linear regression correlation with EF as the dependent factor and syntax score, SDS, total blush, blush area, and MPG as the independent factors was performed. A P value of <0.05 was considered to be statistically significant.

Results

The clinical characteristics did not differ significantly between stenosis and CTO. The perfusion indices of total blush, SDS, and syntax score were not statistically significant between the two groups [Tables 1 and 2]. However, left ventricular end diastolic (LVED) was larger in CTO than in stenosis ($P < 0.05$). The patients with stenosis had better MPG than with CTO, $P < 0.05$.

Thirty-three patients tried recanalization therapy while 3 of them had the poor image quality to calculate MPG. The increased MPG was associated with increased total blush, higher syntax score, and EF ($P < 0.05$) [Table 2]. After PCI both the total blush and MPG increased significantly ($P < 0.05$).

PCI was successful in 27 patients. The one who did not try PCI had only mild stenosis. PCI resulted in better perfusion indicated by increased total blush and MPG ($P < 0.05$); however, syntax score, EF, and SDS did not change significantly [Table 3].

Discussion

Since the start of reperfusion therapy, there has been increasing interests in MPI. It was found in some patients the recanalization of the occluded artery did not result in improved left ventricular function.[10] The cardiac muscle might have died already in spite of recanalization. Many studies have evaluated the cardiac muscle viability.[11] SPECT, positron emission tomography, and magnetic resonance imaging remained the most frequently used examination for cardiac muscle viability.[12] However, these examinations are time consuming and expensive. Most importantly, it is impossible to do the myocardial imaging and coronary artery imaging at the same time. MPG is the byproducts of CAG. After contrast injection, the myocardium becomes darker. It is correlated with viable myocardium. Hence, the darker the myocardium,

Table 1: Comparison between CTO and stenosis

Items	Stenosis (*n* = 16)	CTO (*n* = 18)	*P*
Total blush before PCI	4862.07 ± 4273.96	4614.00 ± 3384.14	0.85
Total blush after PCI	7702.43 ± 4388.05	6007.53 ± 5243.77	0.34
Syntax score	15.74 ± 15.01	19.31 ± 10.47	0.43
SDS	13.42 ± 8.36	12.50 ± 9.01	0.77
EF (%)	55.72 ± 8.01	53.82 ± 8.91	0.57
LVED (mm)	43.94 ± 5.17	49.18 ± 7.14	0.05
MPG before PCI	2.00 (1.00, 2.25)	0.00 (0.00, 1.00)	0.01
MPG after PCI	2.00 (1.00, 3.00)	3.00 (3.00, 3.00)	0.02
Age (year)	64.54 ± 8.86	60.78 ± 12.22	0.44
Gender (male/female, *n*)	14/2	15/3	0.25
SAP (*n*, %)	4 (25.00)	4 (22.22)	0.58
UAP (*n*, %)	12 (75.00)	13 (72.22)	0.58
AMI (*n*, %)	1 (6.25)	2 (11.11)	0.55
OMI (*n*, %)	4 (25.00)	8 (44.44)	0.21
Prio CAG (*n*, %)	4 (25.00)	8 (44.44)	0.13
Prio stent (*n*, %)	3 (18.75)	6 (33.33)	0.29
HF (*n*, %)	3 (18.75)	7 (38.89)	0.18
Stroke (*n*, %)	3 (18.75)	2 (11.11)	0.44
Statin therapy (*n*, %)	15 (93.75)	18 (100.00)	0.47
DM2 (*n*, %)	5 (31.25)	7 (38.89)	0.46
RF (*n*, %)	1 (6.25)	1 (5.56)	0.73
Smoking (*n*, %)	6 (37.50)	12 (66.67)	0.22
Family history (*n*, %)	4 (25.00)	4 (22.22)	0.58
Height (cm)	167.63 ± 6.20	169.21 ± 5.42	0.44
Weight (kg)	69.83 ± 8.85	73.89 ± 12.66	0.31
Systolic BP (mmHg)	136.89 ± 18.58	137.36 ± 17.05	0.94
Diastolic BP (mmHg)	75.79 ± 17.19	77.86 ± 9.77	0.67
TnT (μg/L)	0.01 (0.01, 0.07)	0.02 (0.01, 0.03)	0.16
Creatine (μmol/L)	90.01 ± 21.01	82.60 ± 11.81	0.21
BNP (pg/ml)	143.70 (70.06, 249.50)	127.30 (70.95, 476.90)	0.78
HCY (μmol/L)	21.76 ± 12.56	16.20 ± 8.34	0.52
CRP (mg/dl)	0.32 (0.21, 1.15)	0.37 (0.32, 0.47)	0.72
TC (mmol/L)	4.04 ± 0.74	4.16 ± 0.92	0.69
LDL (mmol/L)	2.44 ± 0.70	2.33 ± 1.02	0.73
Hemoglobin (10^{12}/L)	139.89 ± 17.46	148.36 ± 17.19	0.18

EF: Ejection fraction; LVED: Left ventricular end-diastolic volume; SAP: Stable angina pectoris; UAP: Unstable angina pectoris; AMI: Acute myocardial infarction; OMI: Old myocardial infarction; CAG: Coronary angiography; HF: Heart failure; DM2: Type 2 diabetes mellitus; RF: Renal failure; BP: Blood pressure; TnT: Troponin T; BNP: Brain natriuretic peptide; HCY: Homocysteine; CRP: C-reactive protein; TC: Total cholesterol; LDL: Low-density lipoprotein; CTO: Chronic total occlusion; PCI: Percutaneous intervention; SDS: Summed difference score.

the more viable the muscle is. It is now widely accepted as an indicator of viable myocardium. However, the MPG is only a visual estimate. Yang *et al*. used the video densitometry to study the grayscale changes with time after contrast injection into the coronary artery.[5,13] The darker the myocardium, the higher the grayscale, and thus higher the video density. However, the variation of grayscale is too big to be of great significant value according to our own experience. It might be due to panning the table during the procedure or the respiration which contributes to the big variation of the grayscale or density. The computer workstation by Crealife provides the application of blush area calculation. The area of blush can be calculated by hand drawing the polygonal shape. The blush area times the degree of MPG is the total blush in our study.

To investigate the utility of Crealife workstation, the total blush was performed in patients with CAD of different severity. The patients were divided into three groups, stenosis versus CTO, MPG 1, 2 versus MPG 3, and successful versus unsuccessful recanalization. The study clearly demonstrated that the severity and the extent of the coronary lesions were correlated closely with a total blush. After the recanalization, the total blush improved significantly indicated by the larger area of blush and darker myocardial staining. In the methods section, we displayed two groups' figures. Figure 1 shows the total blush in a patient with chronic left anterior descending occlusion. The dashed area represented blush area that was very small in size, and staining was weak despite successful recanalization (a) and the patient had a big anterior infarct (b). Figure 2 shows the total blush with much larger myocardial staining after recanalization. The extent of

Table 2: Comparison between MPG 1, 2 and MPG 3

Items	MPG 1, 2 (*n* = 11)	MPG 3 (*n* = 19)	*P*
Total blush before PCI	3552.83 ± 2461.09	5467.00 ± 4266.17	0.17
Total blush after PCI	3672.08 ± 2589.32	8731.42 ± 5001.73	0.01
MPG before PCI	2.00 (1.00, 2.00)	0.00 (0.00, 1.50)	0.07
MPG after PCI	1.50 (1.00, 2.00)	3.00 (3.00, 3.00)	0.01
Syntax score	23.21 ± 8.20	13.08 ± 13.21	0.03
SDS	15.42 ± 8.84	12.05 ± 8.50	0.30
EF (%)	50.00 ± 10.49	57.56 ± 6.75	0.03
LVED (mm)	47.11 ± 8.58	45.28 ± 5.26	0.50
Age (year)	61.92 ± 12.61	60.05 ± 10.24	0.66
Gender (male/female)	9/2	16/3	0.66
Height (cm)	166.92 ± 6.36	168.89 ± 4.78	0.33
Weight (kg)	69.33 ± 12.67	73.38 ± 9.69	0.32
Systolic BP (mmHg)	132.17 ± 18.05	136.79 ± 17.18	0.48
Diastolic BP (mmHg)	73.58 ± 12.99	78.21 ± 14.56	0.38
SAP (*n*, %)	5 (45.45)	3 (15.79)	0.12
UAP (*n*, %)	7 (63.64)	15 (78.95)	0.20
AMI (*n*, %)	2 (18.18)	1 (5.26)	0.33
OMI (*n*, %)	5 (45.45)	6 (31.58)	0.42
Prio CAG (*n*, %)	5 (45.45)	7 (36.84)	0.54
Prio stent (*n*, %)	4 (36.36)	4 (21.05)	0.36
HF (*n*, %)	4 (36.36)	6 (31.58)	0.61
Stroke (*n*, %)	2 (18.18)	3 (15.79)	0.66
Statin therapy (*n*, %)	11 (100)	18 (94.74)	0.61
DM2 (*n*, %)	6 (54.55)	6 (31.58)	0.26
RF (*n*, %)	1 (9.09)	1 (5.26)	0.63
Smoking (*n*, %)	7 (63.64)	9 (47.37)	0.57
Family history (*n*, %)	3 (27.27)	4 (21.05)	0.57
TnT (μg/L)	0.02 (0.01, 0.12)	0.01 (0.01, 0.02)	0.06
Creatine (μmol/L)	85.01 ± 16.59	87.78 ± 20.36	0.70
BNP (pg/ml)	222.50 (76.99, 1239.00)	142.70 (64.90, 238.40)	0.21
HCY (μmol/L)	19.47 ± 16.4	21.31 ± 10.47	0.83
CRP (mg/dl)	0.40 (0.21, 0.47)	0.32 (0.26, 0.53)	0.68
LDL (mmol/L)	2.74 ± 1.23	2.25 ± 0.87	0.20
Hemoglobin (10^{12}/L)	143.92 ± 19.2	144.53 ± 18.46	0.93

MPG: Myocardial perfusion grade; PCI: Percutaneous intervention; SDS: Summed difference score; EF: Ejection fraction; LVED: Left ventricular end-diastolic volume; BP: Blood pressure; SAP: Stable angina pectoris; UAP: Unstable angina pectoris; AMI: Acute myocardial infarction; OMI: Old myocardial infarction; CAG: Coronary angiography; HF: Heart failure; DM2: Type 2 diabetes mellitus; RF: Renal failure; TnT: Troponin T; BNP: Brain natriuretic peptide; HCY: Homocysteine; CRP: C-reactive protein; LDL: Low-density lipoprotein.

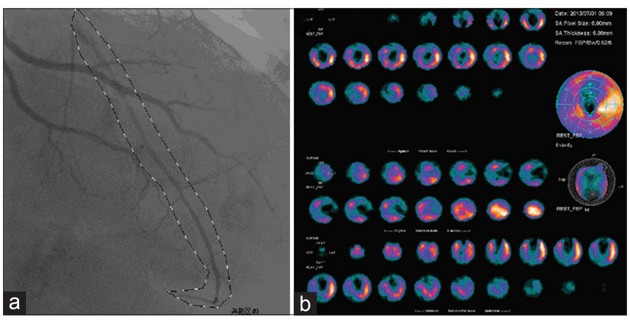

Figure 1: Total blush in a patient with chronic left anterior descending occlusion. The dashed area was blush area which was very small in size, and staining was weak despite successful recanalization (a). The patient had a big anterior infarct (b).

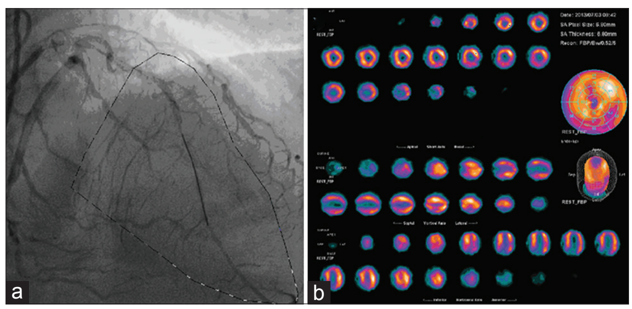

Figure 2: Total blush was much larger after recanalization (a). The extent of the ischemia was small (b).

the ischemia by SPECT was small. It was not clear if the total blush was superior to the simple MPG.[1] Theoretically, the blush grade does not take into account the area of the blush. Therefore, the total blush should have been better. PCI had a significant impact on myocardial perfusion. After PCI both the total blush and MPG increased significantly. At present, we only know that the perfusion was better, LVED smaller and EF higher after PCI. However, more multi-center control

Table 3: Comparison between successful and unsuccessful PCI

Items	Successful (*n* = 27)	Unsuccessful (*n* = 6)	*P*
Total blush after PCI	7738.48 ± 4931.10	2750.00 ± 1291.18	0.02
Total blush before PCI	5080.80 ± 4025.65	3247.83 ± 1787.83	0.29
MPG before PCI	1.00 (0.00, 1.75)	2.00 (1.25, 2.75)	0.08
MPG after PCI	3.00 (2.75, 3.00)	1.00 (0.25, 1.75)	0.01
Syntax score	14.92 ± 13.55	21.67 ± 3.50	0.24
SDS	12.41 ± 8.97	15.67 ± 6.15	0.41
EF (%)	55.52 ± 8.64	53.75 ± 8.54	0.71
LVED (mm)	45.64 ± 6.10	45.75 ± 8.34	0.97
Age (years)	60.33 ± 10.09	64.33 ± 14.26	0.42
Gender (male/female)	23/4	5/1	0.66
SAP (*n*, %)	5 (18.52)	3 (50.00)	0.14
UAP (*n*, %)	21 (77.78)	3 (50.00)	0.19
AMI (*n*, %)	3 (11.11)	0 (0.00)	0.54
OMI (*n*, %)	8 (29.63)	3 (50.00)	0.31
Prior CAG (*n*, %)	9 (33.33)	3 (50.00)	0.37
Prior stent (*n*, %)	6 (22.22)	2 (33.33)	0.46
HF (*n*, %)	7 (25.93)	3 (50.00)	0.25
Stroke (*n*, %)	4 (14.81)	1 (16.67)	0.66
Statin therapy (*n*, %)	26 (96.30)	6 (100.00)	0.82
DM2 (*n*, %)	8 (29.63)	4 (66.67)	0.11
RF (*n*, %)	1 (3.70)	1 (16.67)	0.34
Smoking (*n*, %)	14 (51.85)	4 (66.67)	0.14
Family history (*n*, %)	6 (22.22)	2 (33.33)	0.46
Height (cm)	168.63 ± 6.00	166.5 ± 5.17	0.43
Weight (kg)	71.71 ± 10.25	70.83 ± 13.36	0.86
Systolic BP (mmHg)	137.56 ± 17.34	130.67 ± 21.14	0.40
Diastolic BP (mmHg)	77.78 ± 13.26	74.00 ± 18.62	0.56
TnT (μg/L)	0.01 (0.01, 0.02)	0.03 (0.02, 0.17)	0.06
Creatine (μmol/L)	85.72 ± 18.90	89.77 ± 16.50	0.63
BNP (pg/ml)	142.70 (67.48, 243.95)	157.80 (68.45, 1861.25)	0.64
HCY (μmol/L)	0.52 ± 0.55	4.50 ± 8.20	0.03
CRP (mg/dl)	0.32 (0.15, 0.47)	0.44 (0.34, 12.72)	0.18
LDL (mmol/L)	2.39 ± 1.02	2.78 ± 0.95	0.40
Hemoglobin (10^{12}/L)	146.30 ± 16.62	135.83 ± 22.34	0.20

PCI: Percutaneous intervention; MPG: Myocardial perfusion grade; SDS: Summed difference score; EF: Ejection fraction; LVED: Left ventricular end-diastolic volume; SAP: Stable angina pectoris; UAP: Unstable angina pectoris; AMI: Acute myocardial infarction; OMI: Old myocardial infarction; CAG: Coronary angiography; HF: Heart failure; DM2: Type 2 diabetes mellitus; RF: Renal failure; BP: Blood pressure; TnT: Troponin T; BNP: Brain natriuretic peptide; HCY: Homocysteine; CRP: C-reactive protein; LDL: Low-density lipoprotein.

studies need to be performed to see if the results could be repeated by other investigators.

EF was the gold standard for left ventricular systolic function and had a strong prognostic implication.[14] We performed multivariate linear correlation with EF as the dependent factor and syntax score, SDS, total blush, blush area, and MPG as the independent factors [Table 4]. This model had a high degree of correlation ($R = 0.87$). The syntax score, SDS, total blush, and blush area correlated well with EF, but the MPG correlated less well with EF. The syntax score was a well proven and accepted indicator of the complexity of CAD.[9] It had a strong prognostic implication. The SDS by SPECT also correlated well with the long-term prognosis. The prognostic implication of the MPG had been demonstrated here in this study. The total blush was a new indicator of myocardial perfusion, whether this could lead to an increase in EF remained to be seen in the follow-up.

Table 4: Multivariate linear regression analysis

Indices	Correlation coefficient	*P*
Syntax score	−0.23	0.05
SDS	−0.78	0.03
Total blush	0.01	0.01
Blush area (mm^2)	−0.01	0.01
MPG	1.23	0.53

SDS: Summed difference score; MPG: Myocardial perfusion grade.

In other studies, similar grading system named thrombolysis in myocardial infarction (TIMI) myocardial perfusion (TMP) grade was used.[15] Although the name of the grading system was different, the criteria was, however, similar. The lowest mortality rate was in those patients with TMP grade 3, intermediate in TMP grade 2, and highest in TMP grades 0 and 1. In Steigen TK's study, MPG 0/1 post-PCI had a lower LVEF and a higher heart rate at 1-year follow-up.[1] In patients with ST-elevation myocardial infarction and TIMI grade 3 flow after primary PCI, MPG ≤2 was associated with poor myocardial salvage, a larger infarct, and higher 5-year mortality rate than MPG = 3.[16]

Although our results indicate an association between total blush and myocardial perfusion, the present study was not a prospective cohort design in nature, and it had only small sample size of a single center with significant gender bias. In the further study, more cases from multicenters would be recruited.

In conclusion, the calculation of CAG total blush can be accomplished by a specialized computer which can provide important information on myocardial perfusion and left heart function.

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Conflicts of interest

There are no conflicts of interest.

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