



## Research paper

## Systematic assessment of procedural parameters, influence on downstream testing and 12-month outcomes of a CT-myocardial perfusion service

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## ABSTRACT

**Aims:** This study describes the real-world referral pattern of patients to a CT myocardial perfusion service, the technical issues associated with providing the service, the results of the studies, and the subsequent downstream utilization of other investigations, and patient outcomes.

**Methods and results:** 115 consecutive patients underwent CTA, dynamic rest and dipyridamole-stress perfusion scanning. There were 29 (25%) and 14 (12%) patients who had reversible defects and fixed defects respectively, indicating abnormal flow reserve and previous infarction respectively. In the patients with fixed defects, delayed hyperenhancement was noted in all, indicative of prior infarction, scarring and non-viability. With the existing CTA Appropriateness Criteria, the categorization of “Appropriate,” “Of Uncertain Appropriateness”, and “Inappropriate” would have been applied to 25%, 25% and 50% of the present studies respectively. Up to 72% could have been referred for ischemia evaluation with other modalities of functional imaging after the non-diagnostic CT angiogram. Follow up was complete in 113 subjects (98%) over a period of  $14 \pm 8$  months. In the 29 patients with abnormal flow reserve and CAD, 62% underwent invasive angiography and 94%, angioplasty within a 90-day period. In the patients who underwent angioplasty, all remained free of myocardial infarction or death and 88% remained free of myocardial infarction, death or readmission over a mean of  $14 \pm 8$  months. **Conclusion:** A CT-myocardial perfusion service provided measures of ischemia and infarct detection over that of CTA alone. The information was utilized clinically by doctors to support a strategy of referral to revascularization versus conservative medical management.

## 1. Introduction

Coronary CT angiography (CTA) has a high sensitivity and positive predictive value for the detection of coronary artery disease (CAD). These qualities have been leveraged upon for the exclusion of CAD in patients with low to intermediate pretest probability of CAD presenting with chest pain<sup>1</sup>. However, its utility in the assessment of disease in individuals with existing CAD and high pretest probability has been hindered by the lower specificity and positive predictive value in this group. This is partly due to issues specific to the technique such as partial volume averaging effects in the presence of calcified lesions or previous stent implantation.<sup>2,3</sup> There is also an imprecise correlation between the anatomical appearance of an atherosclerotic lesion and its functional significance in causing ischemia.<sup>4</sup> The limitations of a purely anatomical assessment have been reflected in Appropriate Use Guidelines with CTA being given an Inappropriate or Uncertain classification

in the evaluation of chest pain in patient with known CAD, or in patients with previous stenting.<sup>3</sup> In these clinical scenarios, the utility of downstream testing, therapeutic decision-making and patient outcomes are largely influenced by the availability of functional information, which up to this point in time, CTA has not been able to provide. It is in such situations that techniques such as SPECT & PET imaging, stress-echo, stress MRI and invasive fractional flow reserve (FFR) studies are well-established and widely used. These techniques provide functional information regarding the presence or absence of myocardial ischemia, and have extensive literature documenting the correlation of test results with patient outcomes.<sup>4–10</sup>

The last 8 years have seen an emergence of functional evaluation of atherosclerotic disease by CT techniques such as CT myocardial stress perfusion imaging (CTP) imaging, FFR-CT and TAG (transluminal attenuation gradient).<sup>11–15</sup> This has facilitated the incremental detection of abnormal flow reserve, and allowed the assessment of ischemia and

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**List of abbreviations**

Coronary artery disease CAD  
 Calcium score CaSc  
 Coronary CT angiography Coronary CTA  
 Coronary Artery Disease Reporting and Data System CAD-RADS  
 Heart rate HR

Left ventricle LV  
 Myocardial CT perfusion Myocardial CTP  
 Myocardial CT delayed enhancement Myocardial CTDE  
 Myocardial blood flow MBF  
 Myocardial infarction MI  
 Percutaneous coronary intervention PCI

infarction, to a degree not previously possible in CT studies. Such evaluation is complementary to the anatomical information afforded by CTA and may potentially expand the utility of cardiac CT imaging to answer many more clinical questions. If implemented in clinical practice, many of these techniques also hold the potential to change the way patients are evaluated in the CT-suite, with implications for scheduling and workflow in a busy practice. There may also be potential changes in the down-stream utilization of healthcare resources and healthcare costs as clinical decision-making may be affected.

Our hospital established a clinical CT-perfusion service 24 months ago. The goal of this study is to describe the real-world referral pattern of patients to the service, the technical issues associated with providing the service, the results of the studies, and the subsequent downstream utilization of invasive angiography, and patient outcomes.

**2. Methods**

**2.1. Patient population and preparation**

The service was established in Oct 2016. The experience with 115 consecutive patients from who were successfully scanned from Oct 2016 to Jul 2018 is reported (Graph 1). Referral patterns to the service were tracked, as were the indications for the study, demographic patterns of the patients, scan imaging parameters, radiation dose, scan results, subsequent downstream utilization of cardiac investigations or therapies, correlation of results with invasive angiography (if any) within a 3-month period of the study. Written informed consent was

obtained from each patient, and data was prospectively collected as part of the Institution's quality assurance program.

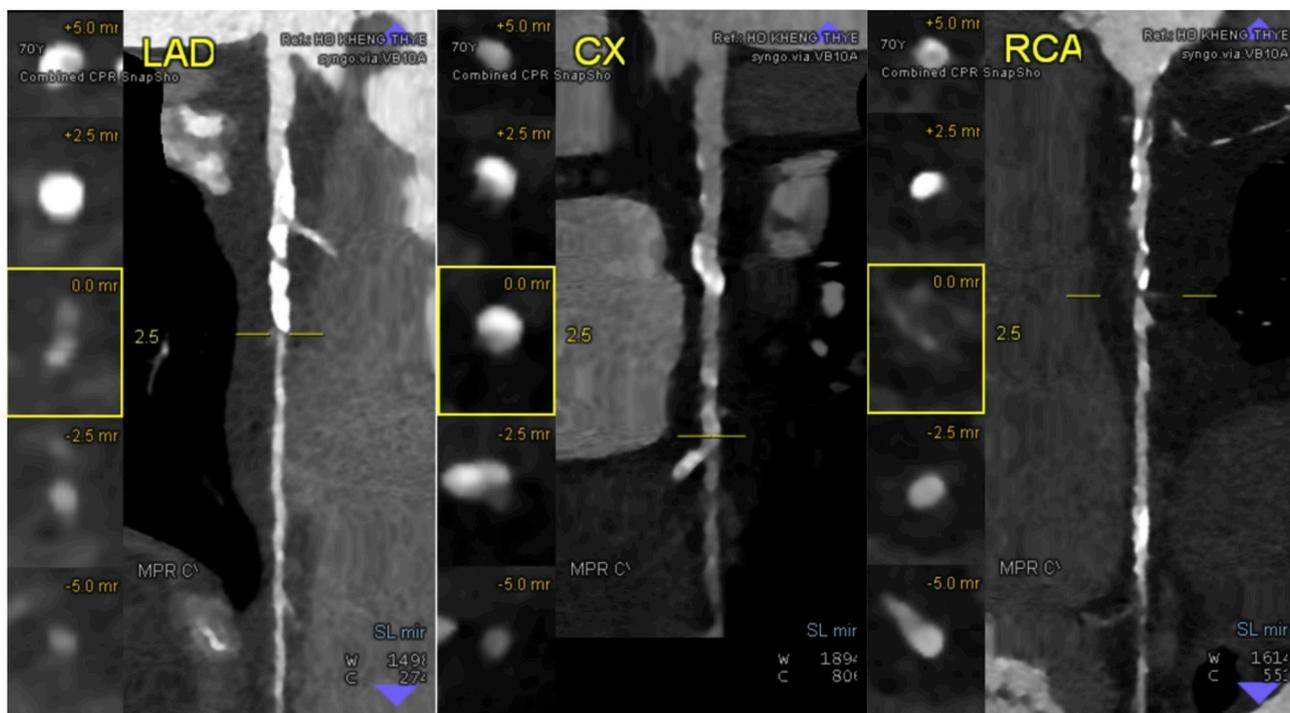
Patients referred to the study were first screened for contraindications.<sup>14,15</sup> They were instructed to withhold the use of beta-blockers and caffeine for 72 h and 12 h respectively, prior to the investigation. Patients were counseled regarding scan duration, and breath-hold instructions prior to the procedure.

**2.2. Imaging protocol**

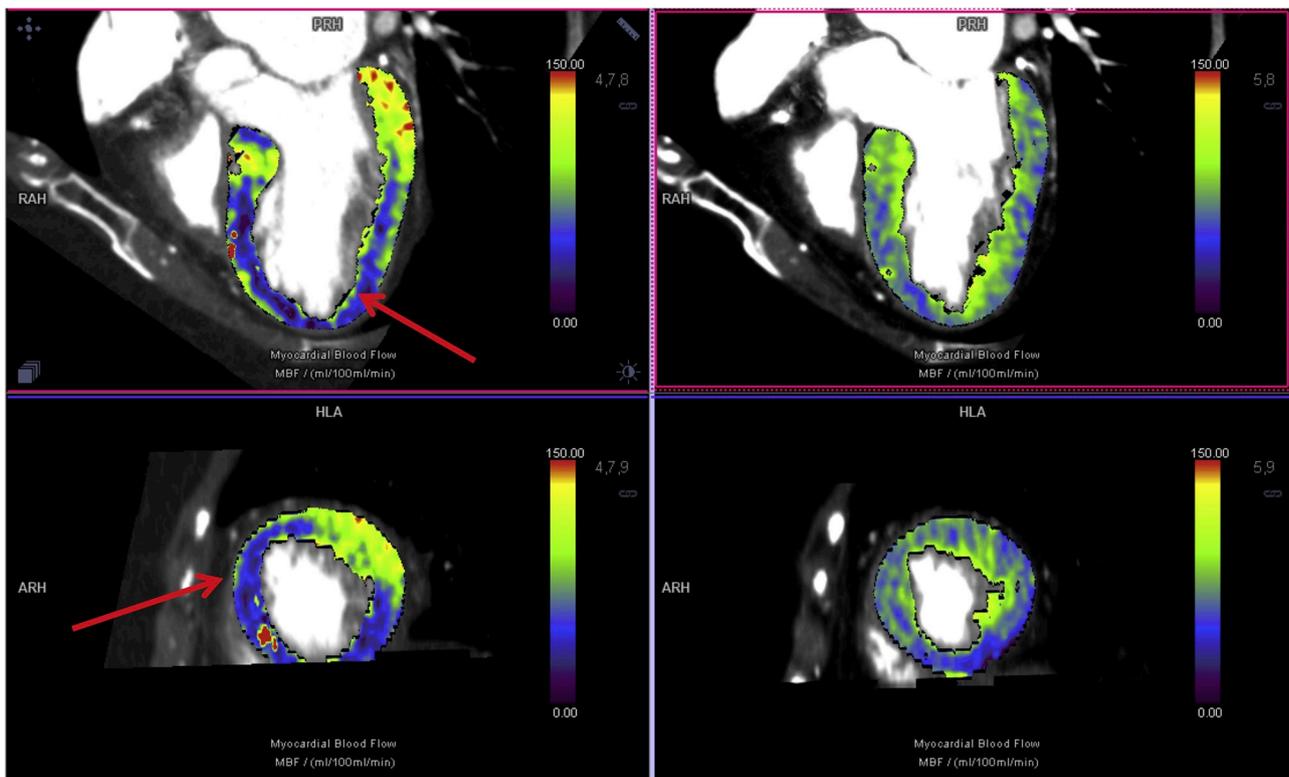
This has been previously described.<sup>14–17</sup> A CT coronary angiogram was first performed. Patients were instructed on the imaging procedure and breath-hold commands. Following a topogram of the chest, a low-dose ECG-gated scan was obtained. The perfusion scan ranges were adjusted over the LV myocardium. ECG, heart rate, and blood pressure were monitored during the procedure. Contrast (Omnipaque 350) was loaded into a power injector (Medrad Stellant). Rest perfusion images of the LV were acquired with injection of 50 ml of contrast followed by 50 cc saline at 5 ml/min. The scan commenced 4 s before arrival of contrast in the LV. The scan duration was 30 s.

**2.3. CT perfusion imaging**

All acquisitions from Oct 2016 to Jul 2017 were performed on a 2nd generation dual-source CT scanner (Definition FLASH, Siemens Healthcare), thereafter all studies were performed on the third generation scanner (FORCE, Siemens Healthcare). Time attenuation curves



**Fig. 1A.** CTA of a 72-year old Chinese female who presented with easy fatigability, but no angina. The Calcium Score was 1724, and there were heavily calcified plaques involving the LAD, LCx and RCA. CAD-RADS 4A.



**Fig. 1B.** CT myocardial perfusion demonstrated a large area of abnormal flow reserve involving the anterior wall, septum and inferior wall (red arrows). This was consistent with severe coronary artery disease involving the LAD and RCA territories. A steal-phenomenon was noted in the inferior wall and the septum, with a flow reserve of 0.74 and 0.69 respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(TACs) for each voxel of the target tissue were acquired. This represents the change of contrast concentration in the tissue with time following the contrast injection. ECG-triggered axial shuttle mode was used. Repeated acquisition of a volume of 73 mm length (FLASH) and 109 mm length (FORCE) at a HR-dependent sampling rate of one every 2–4s yielded complete TACs of the aorta and LV myocardium during end-systole (FLASH & FORCE gantry rotation time 280 ms, slice collimation  $128 \times 0.6$  mm, 80 kV and 70 kV tube voltage for FLASH and FORCE X-ray tubes respectively, tube current 370mAs/rot respectively).

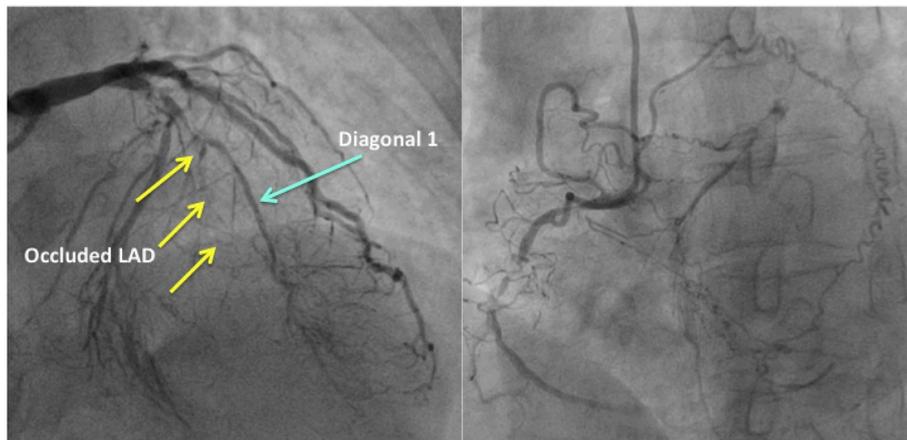
**2.4. Dipyridamole-stress perfusion protocol**

All patients underwent continuous ECG-monitoring. Dipyridamole was infused intravenously at a dose of 0.56 mg/kg/min over a 4-min period. Stress perfusion imaging commenced 3min after completion of

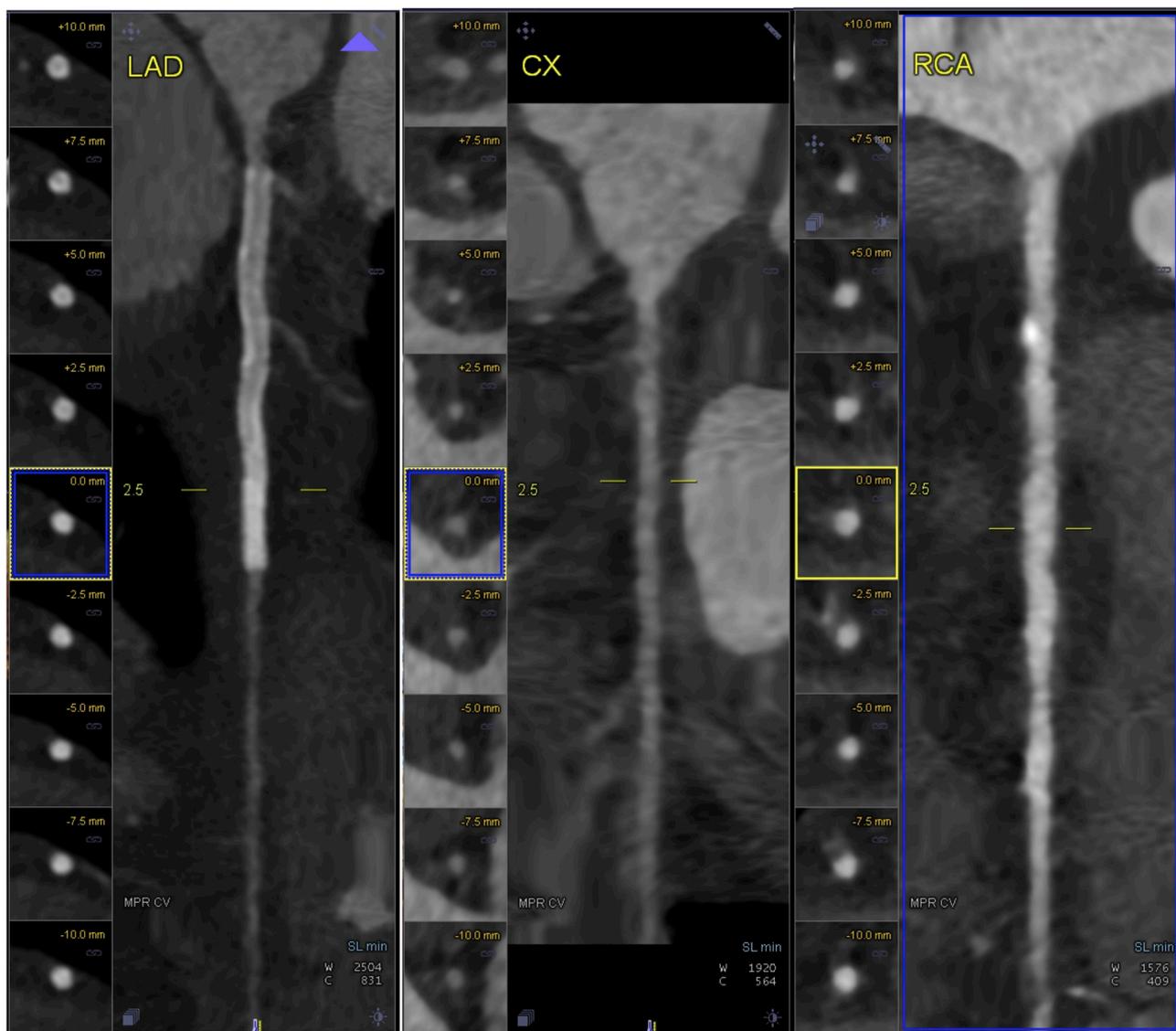
the infusion. The scan was timed to take place during the maximum attenuation based on the TAC in the aorta. Image acquisition for the stress scan was identical to that for the rest scan. The effects of dipyridamole were reversed with intravenous aminophylline (1.5 mg/kg body weight) infused over a 5-min period.

**2.5. Delayed-enhancement scanning**

This was performed in all studies 7min after completion of contrast injection for the stress-scan. End-systolic myocardial delayed enhancement CT images were acquired without additional contrast administration. Tube voltage and tube current setting was 80 kV or 70 kV and 370 mAs.



**Fig. 1C.** Invasive coronary angiography was performed on the basis of the CTA-CTP. This demonstrated triple vessel disease, with complete total occlusion of the mid-RCA and the mid-LAD (yellow arrows), accounting for the steal phenomenon (red arrows, Fig. 1B). The patient underwent revascularization and is well 14 months after the procedure. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2A.** 56-male who presented with an anterior STEMI. He underwent primary angioplasty and stenting to the proximal LAD. He complained of atypical chest pain 2 weeks after the procedure. CTA demonstrated the stent in the LAD, CAD-RADS N (S).

## 2.6. CTA and perfusion image processing and analysis

Image reconstruction was performed with a slice thickness of 3 mm, increment of 2 mm, and a smooth reconstruction algorithm (B22 kernel). A dedicated reconstruction algorithm for myocardial perfusion yielded images with a high temporal resolution, with maintaining CT value stability. MBF was computed from the 4D volume datasets using commercially available software (Volume Perfusion CT Body, Siemens).<sup>18</sup> Post-processing was performed on an offline workstation (SyngoVia, Siemens). A motion correction algorithm was applied. Parametric deconvolution was used to fit a TAC model to the time series of attenuation values for each voxel of the myocardium and the descending aorta. This was used as the arterial input function, yielding a 3D CT dataset for the myocardium with intensity values representing MBF (ml of blood/100 g of tissue/min). The R-R window used for LVEF calculation was from 35% to 75% of the cardiac cycle.

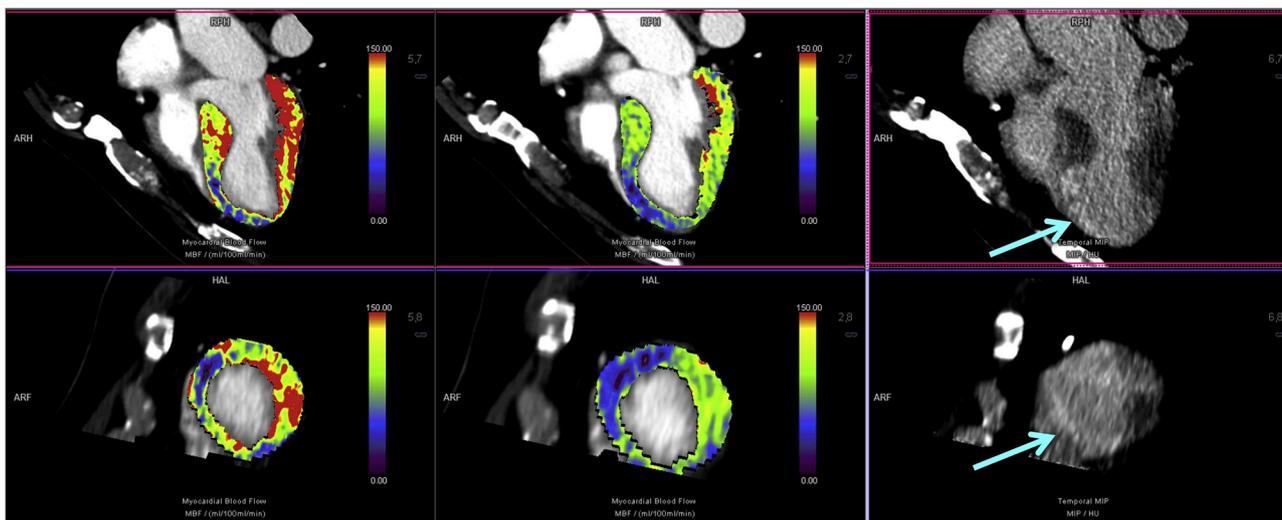
## 2.7. Image reconstruction and data evaluation

The myocardium was evaluated at the apex, mid-ventricular and basal ventricular levels, and read in standard long- and short-axis reformations. Two readers, with 13 and 8 years experience in reporting

cardiac CT, reviewed the CTAs, rest and stress scans for the presence of perfusion defects, and recorded values of MBF in both rest and stress datasets. MBF was determined in each of the 3 vascular territories by manually placing a region of interest in a representative myocardial region, excluding a 1 mm subendocardial zone directly adjacent to the contrast-filled left ventricle, and a subepicardial zone, to avoid any influence of measurements by beam-hardening or partial volume effects. MBF was computed for the whole ventricle (global LV flow) and also for each of the three vascular territories of the heart. MBF was expressed as ml/100 g/min. The distribution of MBF was then correlated to findings on the CTAs, utilizing the SCCT CAD-RADS classification.<sup>19</sup>

## 2.8. Follow-up

Downstream referral for further stress-imaging, invasive coronary angiography within 90 days of the scan, the occurrence of death, myocardial infarction, the performance of coronary revascularization were assessed within 12 months after the CT acquisition. All patients were contacted on the telephone or were seen during routine followup. Non-fatal myocardial infarction and unstable angina were defined according to the standard definition.<sup>20</sup>



**Fig. 2B.** Stress, rest and delayed enhancement dynamic perfusion study demonstrated delayed enhancement in the LAD territory (anterior wall and septum) (blue arrow). No abnormal flow reserve was detected. This indicated the lack of viability in the infarcted territory, and ruled out ischemia as a cause of chest pain. The patient was reassured and managed conservatively. He has been well and event-free up to 14 months post-scan. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2.9. Statistical analysis

All values were reported as mean ± SD, unless otherwise specified. Statistical analysis was performed using Microsoft Excel 2016. Relative SD was used to demonstrate the degree of variability of MBF. Paired t-tests were used to compare regional MBF within individuals at a single time point, and unpaired t-tests used to compare differences between subjects. Analysis of variance (ANOVA) was used when multiple comparisons were made. Statistical significance was defined by convention as  $p \leq 0.05$ .

3. Results

3.1. Procedural parameters

3.1.1. Duration of examination

The entire examination including calcium scoring, CT coronary angiography, rest and stress CTP took  $41 \pm 7$  min. A delayed enhancement examination, if performed, added a further 7 min to the study.

3.1.2. Hemodynamic parameters during CTP

The average heart rate during rest and stress studies was  $69 \pm 10$  and  $78 \pm 5$  bpm respectively ( $p < 0.05$ ), with a mean increment of 20% during stress. None of the patients received beta-blockers. The rest and stress mean arterial blood pressure was  $75 \pm 23$  and  $69 \pm 23$  mmHg respectively ( $p < 0.05$ ).

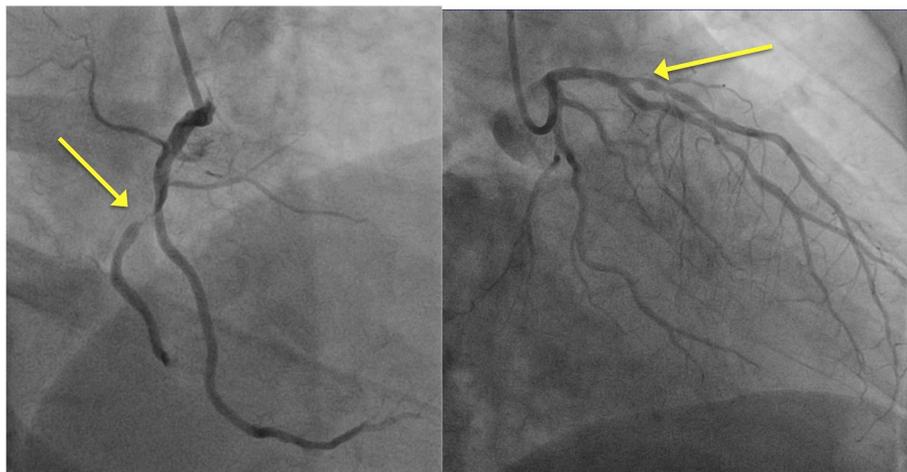
3.1.3. Radiation dose and contrast dose

The combined mean radiation dose for both rest and stress perfusion was  $7.8 \pm 3.2$  mSv. The radiation dose for the 2nd (78 patients) and 3rd generation (37 patients) dual source scanner was  $6.9 \pm 2.1$  mSv and  $8.6 \pm 3.7$  mSv respectively ( $p < 0.01$ ). The mean radiation dose for the CTA was  $2.3 \pm 1.0$  mSv, and this study allowed for functional evaluation of resting LVEF and rest regional wall motion abnormalities. All patients received 50 cc of contrast (Omnipaque 350) each for CTA, rest and stress CTP.

3.2. Patient results

3.2.1. Demographics (Table 1)

123 consecutive patients were referred to the service in a 21-month



**Fig. 3A.** 49-year-old male with presented acutely with an inferior STEMI. Primary PCI was performed to the culprit mid-RCA. There was an intermediate lesion noted in the LAD.

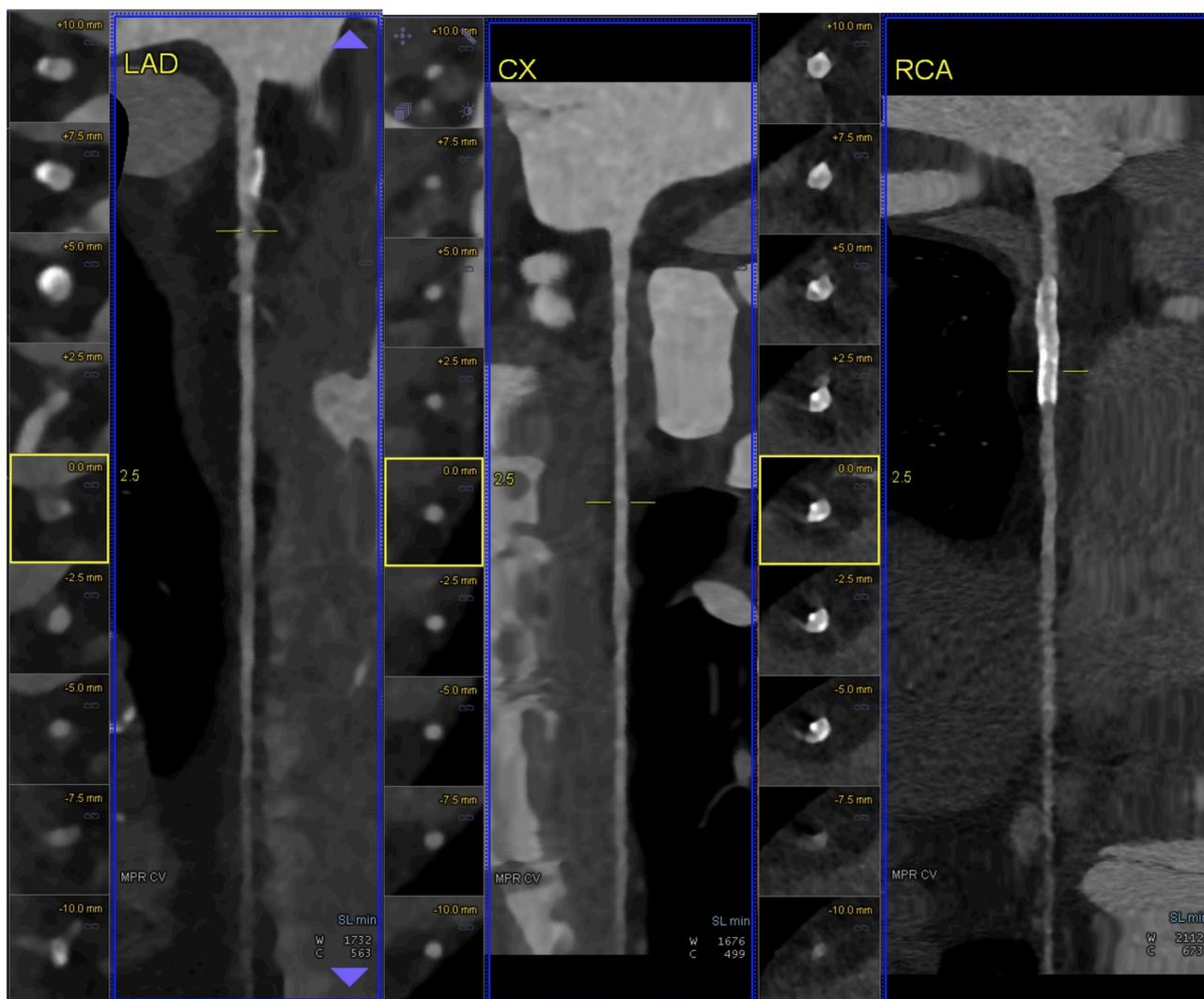


Fig. 3B. CTA demonstrated a patent stent in the RCA, and a 50%–69% lesion in the proximal LAD.

period by cardiologists (Graph 1). Seven patients were not suitable for the study. Two were in atrial fibrillation, two could not maintain satisfactory breathhold, one developed back pain during the scan which had to be aborted, another developed confusion after initial contrast injection and one was found to have an asymptomatic chronic aortic dissection during the scout scan. We report on the experience with 115 patients (age  $62 \pm 10$  years, 89% males). 38 (33%) had diabetes, 32 (64%) had a history of previous CAD, with 60 (52%) having undergone previous revascularization (see Table 1).

### 3.2.2. Calcium score & CT coronary angiography results

In 44 patients (38%) without previous revascularization, the CaSc was  $357 \pm 120$  (range 0–3638). In 23 (20%) patients, excluding patients with stents, the CTA was coded as non-diagnostic in at least one of the vessels (CAD-RADS N). In the remaining 92, all the images were of diagnostic quality and readers assigned a CAD-RADS grading of 3, 4 and 5 in 17 (19%), 11 (12%), 7 (8%), respectively (Table 2).

### 3.2.3. Categorization of utility of CT angiography with existing Appropriate Use Guidelines

There were 84 (73%) patients who had CAD, as evidenced by median calcium scores of  $357 \pm 120$ , a history of previous stenting procedures, or of CAD. 50% of our patients had previous stent-insertion; 95% of which had a stent diameter < 3 mm, with none of the stents implanted in the left main coronary artery. With the existing

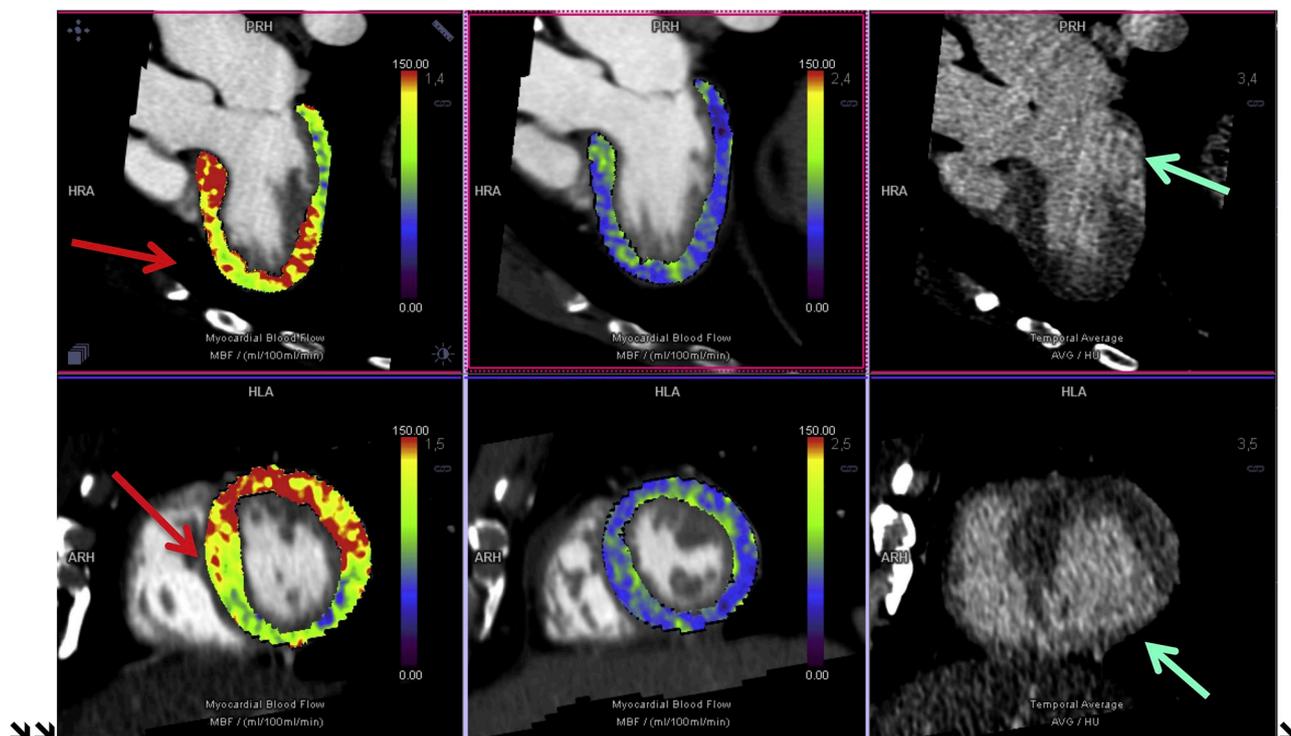
Appropriateness Criteria, the categorization of “Appropriate,” “Of Uncertain Appropriateness,” and “Inappropriate” would have been applied to 25%, 25% and 50% of the present studies respectively. Up to 72% could have been referred for ischemia evaluation with other modalities of functional imaging, based on CTA or appropriateness criteria, after the non-diagnostic CT angiogram.<sup>5,6,8</sup> In this study, demonstration of ischemia, and clarification of non-diagnostic or uncertain CTAs, was provided by CTP; 23 (20%) and 21 (18%) had a CAD-RADS (N), and 3 to 5 classification respectively.

### 3.2.4. Indications for CT-perfusion (Table 2)

The most common indication was the detection of ischemia in coronary segments unevaluable by CTA, usually due to extensive calcification and blooming artifact from stents (50%). Other indications included evaluation of vessels coded CAD-RADS 3, 4 and 5 (18%), and the evaluation of viability (16%).

### 3.3. CT perfusion results

115 patients successfully underwent rest-stress perfusion imaging. All subjects with a fixed defect also underwent delayed-enhancement scanning. There were 29 (25%) with reversible defects, indicating the presence of abnormal flow-reserve (Figs. 1 and 3), and 14 (12%) had fixed defects, indicating previous infarction. In the patients with fixed defects, delayed hyperenhancement was noted in all indicative of prior



**Fig. 3C.** CT perfusion demonstrated delayed hyperenhancement and hypokinesia was noted (Video S3) in the interior wall (blue arrows), consistent with infarction and an absence of viability in the RCA territory. Abnormal flow reserve was detected in the septum (red arrows), consistent with a hemodynamically significant lesion in the proximal LAD. On the basis demonstration of ischemia, the patient was scheduled for revascularization of the LAD. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

infarction, scarring and non-viability (Figs. 2 and 3, Video S3). All infarcts were transmural in extent. The global rest and stress blood flow was  $83.76 \pm 33.67$  ml/100 g/min &  $137.70 \pm 47.28$  ml/100 g/min respectively, with a coronary flow reserve of  $1.67 \pm 0.37$ . In segments with abnormal flow reserve and fixed defects, the stress, rest blood flow and coronary flow reserve was  $98.17 \pm 29.10$  ml/100 g/min,  $73.50 \pm 18.79$  ml/100 g/min and  $1.40 \pm 0.49$ . A steal-phenomenon was noted in 6 (5%) patients, with a CFR < 1, indicative of severe disease or complete total occlusion (Fig. 1).

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.jcct.2019.04.006>

### 3.4. Follow-up results

#### 3.4.1. Downstream cardiovascular events

Follow up was complete in 113 subjects (98%) over a period of  $14 \pm 8$  months. In the patients who had only fixed defects or normal perfusion scans, over the follow-up period, none sustained myocardial infarction or cardiac death.

#### 3.4.2. Downstream referral to invasive angiography and subsequent management

In the 29 patients (25%) who were found to have abnormal flow reserve and CAD on CTA, 18 (62%) underwent invasive angiography and 17 of these 18 (94%), angioplasty within a 90-day period. In the patients who underwent angioplasty, all (100%) remained free of myocardial infarction or death and 88% remained free of myocardial infarction, death or readmission over the period of  $14 \pm 8$  months. Of the 11 who were managed medically (with more aggressive lipid lowering, antiplatelet and betablocker therapy<sup>21</sup>), 4 had known disease of small branch vessels, 3 had non-vascular territory defects, and 4 declined invasive management of whom 2 subsequently underwent PCI for worsening angina (after the 3-month period) despite maximal medical therapy. Of those who were found to have normal perfusion or

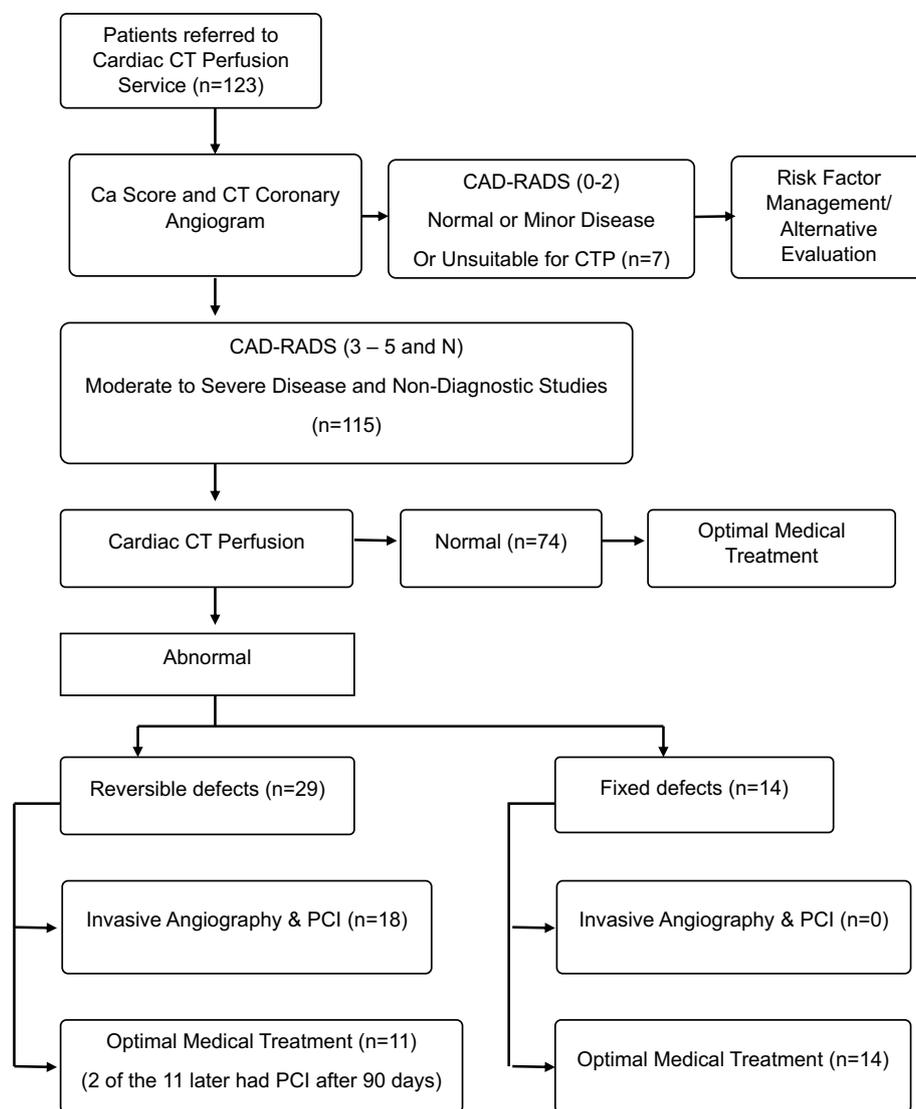
fixed defects, only one patient with a fixed defect underwent invasive coronary angiography and angioplasty. Patients with a documented steal-phenomenon on CTP demonstrated severe (95%) CAD or complete total occlusion (CTO) on invasive angiography.

## 4. Discussion

In real-world practice, the current noninvasive technologies used for diagnosis and risk stratification in stable elective patients prior to invasive angiography do not perform at published diagnostic levels, as evidenced by the low rates of obstructive CAD at elective catheterization.<sup>22</sup> When applied to high-risk patients with known CAD, CT-angiography has a lower specificity due to non-diagnostic results arising from the presence of heavily calcified plaques or previous stenting procedures.<sup>3,23</sup>

### 4.1. Patient population & indications for testing

This population would not have been typically referred to perform a CTA. CTA's strength is in the evaluation of low to medium-risk cohorts for CAD. With the existing Appropriateness Criteria,<sup>3</sup> 75% of the present studies would have been deemed of Uncertain Appropriateness or Inappropriate. Previously, many would not have undergone CTA and if they had, this would have been followed by referral to other modalities of functional imaging (5, 7, 8). Twenty-three (20%) and 21 (18%) had a CAD-RADS (N), and CAD-RADS 3 to 5 classification respectively. CAD-RADS 3 to 5 are combined as 1 category as the guidelines recommend further functional imaging or invasive angiography in these groups.<sup>19</sup> In addition, 50% had previous stent-insertion, 95% of which had a stent diameter of less than 3 mm. It has been suggested that both these groups should undergo functional or viability assessment.<sup>19</sup> In this study, demonstration of ischemia, and clarification of non-diagnostic or uncertain CTAs, was provided by CTP. Enough information was obtained through this strategy so that clinicians did not order further



Graph 1. CT Perfusion service workflow.

Table 1 Patient characteristics.

Table 1	Patient Characteristics
Age (years)	62 ± 10
Male	102 (89%)
<b>Race</b>	
Chinese	94 (82%)
Malay	1 (1%)
Indian	7 (6%)
Others	13 (11%)
Body-mass Index (kgm <sup>-2</sup> )	25.8 ± 4.5
<b>Cardiac Risk-factors</b>	
Diabetes	38 (33%)
Hypertension	62 (54%)
Hyperlipidaemia	99 (86%)
Smoker	20 (17%)
<b>Cardiac Status</b>	
Prior Myocardial Infarction	24 (21%)
Previous coronary stenting/coronary bypass	60 (52%)

stress-imaging. In our cohort, functional testing was successfully provided purely by CTP, as a branch-point in the triaging strategy prior to ICA.

#### 4.2. Utility of results

Our findings suggest that in our institution, the CTA-CTP results are being utilized to guide patient management. With the demonstration of both ischemia and anatomic disease, the patient is more likely to undergo invasive angiography and revascularization. In comparison, the patients without ischemia are being managed medically<sup>21</sup> without an excess outcome of cardiac death or MI in a 1-year period. While such an ischemia-driven approach is commonly used in strategies such as nuclear and echo stress-imaging, this has not been widely documented in the setting of cardiac CT stress-imaging. The combination of anatomical and functional data appears to be useful to clinicians in the post-test management of patients. This is possibly indicated by the low and higher invasive angiography rates in patients without and with demonstrable ischemia on CTP. In this regard, the integrated anatomic and functional imaging achieved by the CTA-CTP combination appears to be functioning as a gatekeeper.

#### 4.3. Correlation of CTA/CTP results with invasive angiography/PCI results

When a steal phenomenon was reported on CTP (stress-flow less than the rest-flow), there was either complete occlusion or severe stenosis (> 90%) on ICA of the corresponding artery. The documentation

**Table 2**  
Indications for CTP.

	Indications	Frequency (%)
1	Demonstration of AFR in intermediate lesions on CTA (CAD-RADS 3)	9 (8)
2	Evaluation of AFR in severe stenosis or suspected complete total occlusion (viability assessment) - CAD-RADS 4 & 5	15 (13)
3	Evaluation of CAD-RADS Vulnerable	5 (4)
4	Demonstration of AFR in lesions unevaluable on CTA CAD-RADS (N)	23 (20)
5	Evaluation of patients after coronary stent-insertion ( $\leq 3$ mm) CAD-RADS S	57 (50)
6	Evaluation of flow-reserve in CCS $> 1000$	2 (2)
7	Evaluation of viability	18 (16)
8	Evaluation of flow-reserve in patients with risk-factors	23 (20)
9	Preoperative coronary risk assessment prior to non-coronary cardiac surgery with intermediate to high risk of CAD	1 (1)
10	Risk assessment post-CABG more than 5 years	2 (2)
11	Evaluation of new-onset heart failure in the presence of CAD detected on CTA (extent of ischemia evaluation)	1 (1)

\*The frequencies are not mutually exclusive.

of the phenomenon is a strength of dynamic perfusion imaging, and the quantitation of flow provides important information that can be used for pre-procedural planning. PCI of such vessels is more complex, may require longer procedure times, and is associated with higher risks compared to simpler lesions.<sup>24</sup>

#### 4.4. Integration of anatomic and functional cardiac imaging

In this study, 62% of patients with demonstrable ischemia underwent subsequent angiography, and 94% of those underwent revascularization (PCI). The proportion undergoing angiography was relatively low, but such patients were more likely to undergo angioplasty than those with normal perfusion or documented infarction without ischemia. In addition, patients without demonstrable ischemia were free of cardiac death or MI over a 14-month period. This illustrates both the utility and safety of a combined anatomic and ischemia-guided approach in our population.

#### 4.5. Radiation dose

The 25% increase in radiation dose for the combined rest and stress perfusion evaluation in the third generation, compared to the second generation scanners, despite a reduction from 80 kV to 70 kV, is possibly contributed to by the increased scan range of the former. While the increased scan length allows full coverage even in dilated left ventricles, and possibly better diagnostic performance, there appears to be a certain radiation penalty. This observation will require evaluation in future studies. The 70 kV protocol was used to reduce radiation dose, however clinical results have not been previously validated against PET or invasive FFR studies.

#### 4.6. Patient preparation and use of beta-blockers

Due to the concern that beta-blocker utilization would attenuate detection of abnormal flow reserve, all patients were instructed to avoid its utilization 48 h prior to the study. This is contrary to beta-blocker utilization in CTA, where its use improves coronary diagnostic quality. The effect on the sensitivity and specificity of CTP in detecting ischemia remains to be elucidated by later studies.

#### 4.7. Workflow issues

The acquisition of a study (inclusive of CT coronary angiogram, rest and stress perfusion) was completed within  $41 \pm 7$  min. This afforded information regarding coronary anatomy, LVEF, ischemia, infarction and viability within a single setting. The information derived makes the study attractive to clinicians and potentially provides a “one-stop shop” for the evaluation of coronary artery disease. The utility of the approach should be evaluated in multicenter studies.

#### 4.8. Limitations

This was a single-centre registry study. The numbers of patients are limited, but this is to-date the largest single-centre registry cohort reported. As this is a series of real-life patients and not a trial, patients were not mandated by protocol to undergo ICA or other gold-standard testing. Rather, the disposition was left to the professional management of referring physicians. Surrogate measures of test performance, such as the percentage of abnormal studies that underwent invasive angiography and angioplasty, and the rates of hard-events in patients who did not undergo revascularization were used. The referral bias resulting from the above approach limits the generalizability of this observational study. Our findings require further validation with multicenter registries.

Both rest and stress dynamic CTP were performed. While this approach increases the radiation dose modestly (by about 3 mSv compared to stress-alone studies), this allowed the estimation of CFR and quantitation of absolute flow. The utility of such measures and benefits over static stress studies remain to be studied, but appear useful in the documentation of a steal-phenomenon (a marker of severe CAD or CTO Fig. 2) and differentiation between abnormal flow reserve and infarction (Fig. 3). There was no comparison of dynamic CTP against FFRCT, other modalities of stress-imaging (nuclear, echo or MRI), or data on plaque composition. However, this was not the stated purpose of this report.

#### 5. Conclusion

A CT-myocardial perfusion service successfully provided measures of ischemia and infarct detection over that of CTA alone. The information was utilized clinically by doctors to support a strategy of referral to revascularization versus conservative medical management, resulting in positive outcomes in both groups.

#### Conflicts of interest

Dr Ho is on the Siemens Bureau of Speakers, and has previously received honoraria and grants from Siemens Healthineers, but not for this current manuscript. Dr Ong has no conflicts of interests regarding this manuscript. Ms Sharon Ong is a full-time employee of Siemens Healthineers, Singapore.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jcct.2019.04.006>.

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