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Research article

Stress-only dynamic computed tomography perfusion protocol (CTP) alone without computed tomography coronary angiography (CCTA) has limited specificity to diagnose ischemia: A retrospective two-center study

Olga Sliwicka [a], Andrea Baggiano [b,c], Ioannis Sechopoulos [a,d,*], Gianluca Pontone [b,e]

[a] Department of Medical Imaging, Radboud University Medical Center, Nijmegen, the Netherlands
[b] Department of Cardiovascular Imaging, Centro Cardiologico Monzino IRCCS, Milan, Italy
[c] Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy
[d] Technical Medicine Center, University of Twente, Enschede, the Netherlands
[e] Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

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ABSTRACT

Purpose: To investigate diagnostic performance of stress-only dynamic myocardial computed tomography perfusion (CTP) without computed tomography coronary angiography (CCTA) to diagnose ischemia with invasive fractional flow reserve (FFR) as a reference standard.

Method: 135 datasets (68 positive for ischemia with invasive FFR < 0.8) acquired with a 256-slice CT system (Revolution, GE Healthcare, Chicago, IL, USA) were retrieved, postprocessed with a deep learning-based algorithm (Advanced intelligent Clear-IQ Engine (AiCE), Canon Medical Systems, Otawara, Japan) (FC03/cardiac kernel, 8 mm slice thickness), analyzed using a dedicated workstation (Vitrea research 7.11.0. Vital Images, Minnetonka, MN, USA), and loaded into a clinical workstation (CardIQ, GE Healthcare, Chicago, IL, USA) for review. Ten observers with various experience from two research sites evaluated the post-processed images, perfusion slices and maps to indicate presence vs absence of perfusion defect and its probability (five-point Likert scale). Binary decisions and probability scores were used to calculate sensitivity and specificity for each reader, and to create receiver operating characteristics (ROC) curves, respectively. Furthermore, the correlation coefficient (ICC) was computed. ROC AUC of a purely quantitative analysis was obtained thanks to a color-coded map with a fixed scale superimposed on myocardial walls displaying myocardial blood flow (MBF) values.

Results: The overall case-based sensitivity and specificity for the detection of perfusion deficit were 0.79 and 0.30, respectively. No significant differences were detected in the AUC across readers (p value $= 0.66$). The AUC values were 0.50, 0.58, 0.63, 0.59, 0.45, 0.60, 0.56, 0.61, 0.52, 0.61. Absolute reader agreement ICC was 0.60 (good agreement) for an average case.

Conclusion: Dynamic CTP alone has good sensitivity, but low specificity when analyzed without CCTA. These findings reinforce the need to guide the interpretation functional test with the knowledge of coronary artery anatomy.

1. Introduction

Dynamic myocardial CT perfusion (CTP) is a novel imaging technique developed to depict functional information of the cardiac wall, in the hopes of improving the diagnosis of cardiac ischemia. However, its use in clinical practice remains limited. The relatively high radiation dose and scarce diagnostic evidence from prospective trials place dynamic CTP as a second-line stress imaging modality for cardiac application [1]. Nowadays, according to the latest clinical CT guidelines [1], the use of dynamic CTP could be considered to obtain functional information as an alternative to other stress tests, but its precise role still needs to be determined.

In principle, dynamic CTP accompanied by coronary CTA could serve as a gatekeeper for invasive workup [2], since it might reduce unnecessary diagnostic invasive coronary angiography. Dynamic CTP is a cost-effective method with added clinical value for detecting obstructive

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* Corresponding author at: Department of Medical Imaging, Radboud University Medical Center, Geert Grooteplein Zuid 10, 6525 GA Nijmegen, the Netherlands.
E-mail address: ioannis.sechopoulos@radboudumc.nl (I. Sechopoulos).

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coronary artery disease (CAD) in patients with previous stenting with a sensitivity of 0.86–0.96 and a specificity of 0.74–0.84 [3]. Moreover, dynamic CTP has incremental diagnostic accuracy (sensitivity 78%, specificity 73%) for detecting obstructive coronary artery disease [3]. The diagnostic accuracy of dynamic CTP is comparable to that of cardiac magnetic resonance (CMR) and positron emission tomography (PET) with a sensitivity of 93% [82–98% 95% CI interval] and a specificity of 82% [70–91% 95% CI interval] on a patient level [4] and is superior to that of single-photon emission computed tomography (SPECT) [4]. However, the scanning protocol of dynamic CTP requires a sequential performance of the rest and stress protocol regardless of the order (rest first or stress first). Usually, the rest protocol consists of resting perfusion analysis using the coronary CTA dataset, while the stress protocol consists of dedicated stress perfusion scanning. Therefore, the radiation exposure in dynamic CTP varies among protocols and vendors (range of 4.6–12.8 mSv) [5], thus being not negligible. One way to decrease the dose would be avoiding acquisition of the rest protocol (or coronary CTA) and hence performing only the acquisition of the stress dataset. However, the clinical reports on the use of stress-only dynamic CTP are lacking. Therefore, we investigated the diagnostic performance of a stress-only dynamic CTP protocol in patients suspected for ischemia with invasive fractional flow reserve (iFFR) as a reference standard.

2. Material and methods

2.1. Study population

This study took place in two sites: Centro Cardiologico Monzino IRCCS in Milan, Italy and Radboudumc in Nijmegen, The Netherlands. The institutional medical ethics committee approved this retrospective study and waived the requirement for written informed consent since it reuses existing dynamic CTP datasets of patients who participated in the PERFECTION trial [6]. In that study, the patients scheduled for clinically-indicated invasive coronary angiography (ICA) with iFFR were evaluated with coronary CTA, fractional flow reserve computed tomography (FFR_{CT}), and stress dynamic CTP according to the clinical protocol. One-hundred-forty-three consecutive anonymized stress dynamic CTP datasets of adult patients were obtained and retrieved for this study. Nine of these datasets were excluded from the study due to poor image quality and incomplete dataset ($n = 5$), insufficient image quality ($n = 2$), and acquisition failure ($n = 1$). Therefore, a total of 135 datasets were finally selected for the study.

The baseline characteristics of the study population are shown in Table 1.

Table 1
Study population characteristics.

Characteristic	Value
Number of patients	135
Sex (n; %)	26 (20)
Women	109 (80)
Men	
Average age (years, std. dev)	65 ± 8.2
Body weight (kg) (mean; std. dev)	77 ± 12.9
BMI	26 ± 4.1
Average heart rate during dynamic CTP (mean; st. dev)	84 ± 14.2
Scanning parameters	
Radiation dose	
DLP [mGycm]	
Stress CTP effective dose [mSv]	384.5
	5.38
Tube voltage [kV]	100
Average number of beats	25

2.2. Stress dynamic CT perfusion protocol

All 135 stress dynamic myocardial CT perfusion examinations were performed based on the protocol of the PERFECTION Trial in Centro Cardiologico Monzino, Milan, Italy. All images were acquired using a 256-row detector whole-heart coverage scanner (Revolution scanner, GE Healthcare, Chicago, IL, USA), with a fixed dynamic CTP protocol for all patients: 25 consecutive CT samplings with fixed tube voltage (100 kV) and tube current (150 mA) as previously described here [7]. All study patients were administered 140 μg/kg/min of adenosine during a 4-minute-long infusion. The dynamic CT images were acquired at every heartbeat during this time window, resulting in 25 timeframes divided into three packages, with different specification. The scan followed an injection of a patient-specific amount of iodinated contrast agent (Iodixanol 320, Visipaque, GE Healthcare, Oslo, Norway) calculated from the equation: $contrast\ volume = 0.7 \times body\ weight\ in\ kilograms,$ containing 320 mg iodine/ml with a 5.0 ml/s infusion rate. Additional details of the CT acquisition protocol, including radiation dose parameters, are shown in Table 1.

2.3. Image reconstruction

For the present study, the images were reconstructed using the Advanced intelligent Clear-IQ Engine (AiCE) [8] deep learning-based algorithm (Canon Medical Systems, Otawara, Japan) (FC03/cardiac kernel. 8 mm slice thickness) [9] and analyzed using a dedicated workstation (Vitrea research 7.11.0. Vital Images, Minnetonka, MN, USA). The images were post-processed using the Dynamic Myo Perfusion app preinstalled at Vitrea, ensuring the best cardiac axes and contrast phase selections. For each dataset, five images in three imaging planes (four-chamber view, two-chamber view, and short axis views at basal, midventricular and apical level) were obtained. All datasets were loaded into a CardIQ clinical workstation (GE Healthcare, USA) where the perfusion analysis was done using a model for capillary exchange [10,11]. For each dataset, five perfusion slices in three imaging planes (four-chamber view, two-chamber view, and short axis views at basal, midventricular and apical level) and one perfusion map were obtained at CardIQ and used in the reader study. From the resulting datasets, one 16-segment perfusion map was generated also in the CardIQ workstation. An example of the used layout is shown in Fig. 1.

2.4. Multi-reader image evaluation

The anonymized images were assessed by ten readers (five from each site) with different expertise in reading dynamic CTP, involving four experts (two cardiovascular radiologists and two cardiologists with more than five years' experience in reporting cardiac CT), two intermediate (general radiologists with five years' experience), and four beginners (radiology residents with less than five years of (general) radiology experience).

All 135 acquired datasets were evaluated using a custom-made dedicated scoring software displayed on a GE CardiQ and Barco MDSC-12133 workstations at two sites. During a single session (with a minimum 10-minute-long break after one hour), each study observer scored the images of all 135 patients (five time series and one perfusion map per case) in random order. Window Width/Window Level (WW/WL) was pre-set to the default myocardium view recommended by the vendor (150 HU/300 HU) and could not be adjusted. The readers indicated the presence or absence of perfusion defects (ischemia) using a binary decision (yes/no and provided the probability of a perfusion defect (ischemia) present in the images using a five-point Likert scale (A. very high; B. high; C. moderate; D. low; E. very low). All readers were blinded to patient characteristics, rest perfusion, CCTA and invasive assessment.

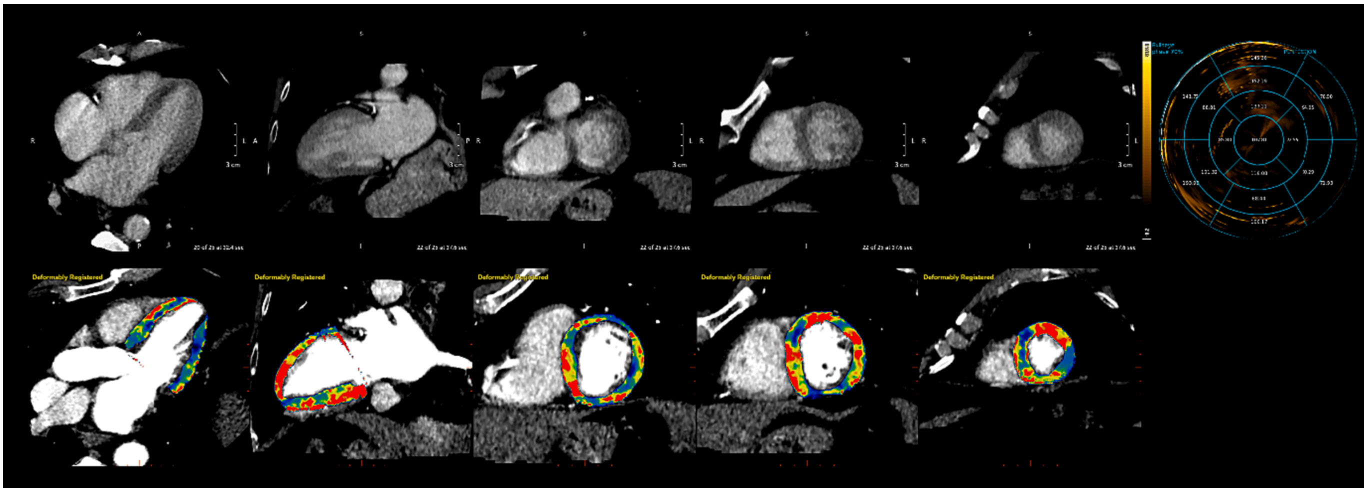

Fig. 1. A study example case. 60-year-old patient with positive invasive FFR. All the readers correctly indicated presence of ischemia (blue). Upper row: 5 raw dynamic CTP images and a perfusion map. lower row: perfusion slices with color-coded map related to MBF calculation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.5. *Quantitative perfusion map evaluation*

Myocardial blood flow (MBF) assessment was displayed with a color-coded map superimposed on myocardial walls characterised by 0 and 150 ml/100 g/min as lowest and highest threshold, respectively. Segments were dichotomized into normally perfused and hypoperfused using a threshold of 100 ml/100 g/min [7].

2.6. *Statistical analyses*

Statistical analysis for perfusion map evaluation was performed using IBM SPSS Statistics 27.0 for Windows (IBM Corporation. Armonk. NY. USA). The means, variances, and mean absolute error of myocardial blood flow results were calculated and underwent analysis of variance (ANOVA).

The binary decision responses were used to calculate sensitivity and specificity for each reader, while from the probability of perfusion deficit scores were used to create receiver operating characteristics (ROC) curves. For all evaluations, the ground truth on presence of ischemia obtained as a part of the PERFECTION trial, which was based on ICA and iFFR, was used as the reference standard.

The receiver operating characteristics (ROC) curves were estimated for all observers in SPSS. The interobserver agreement was evaluated with the intraclass correlation coefficient (ICC) analysis [12] using a two-way mixed model with averaged measures for absolute agreement. The ICC results were rated as < 0.40: poor agreement; 0.40 to 0.59: fair; 0.60 to 0.74: good; and 0.75 to 1.00: excellent [13].

3. Results

3.1. *Reference standard*

Out of all 135 included patients, 68 were positive for ischemia with an iFFR value below 0.8 with flow-limiting stenosis on a patient level.

3.2. *Multi-reader image evaluation*

The average ICC for absolute reader agreement was 0.60 for an average case (good agreement). Fig. 3. shows discrepancies in readers answers.

The ROC curves for each reader and for the average reader are shown in Fig. 2, with their corresponding areas listed in Table 2.

No significant differences were detected in the AUC across readers (p value = 0.66) (Fig. 2). The overall case-based sensitivity and specificity for all readers for the detection of perfusion deficit were 0.79 and 0.30, respectively (Table 3).

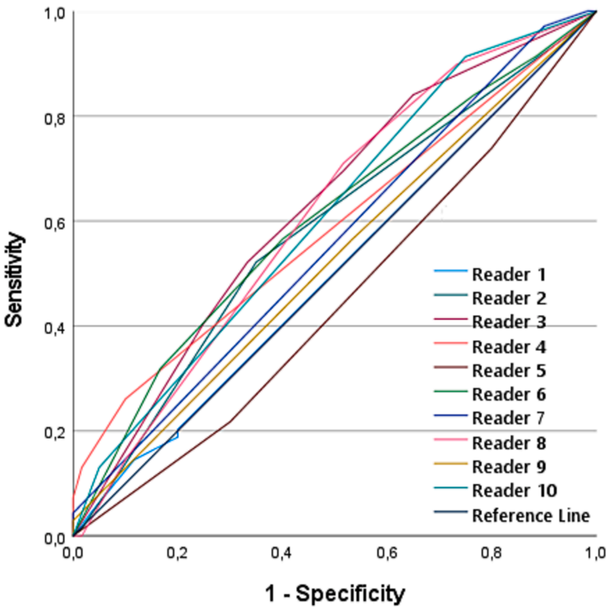

Fig. 2. Receiver operating characteristics curve of each study reader.

3.3. *Myocardial blood flow evaluation*

The MBF results (Table 4) show MBF values differ across patients and display large discrepancies in standard deviation, especially in segment 17 in negative cases, and segment 9 in positive cases. The AUC constructed from the lowest MBF value per perfusion map is shown in Figs. 4.

4. Discussion

The main finding of this study is that dynamic CTP alone does not provide enough diagnostic information to diagnose ischemia caused by flow-limiting stenosis with an iFFR value below 0.8 with a sensitivity and specificity of 0.78 and 0.30, respectively. Previous reports showed

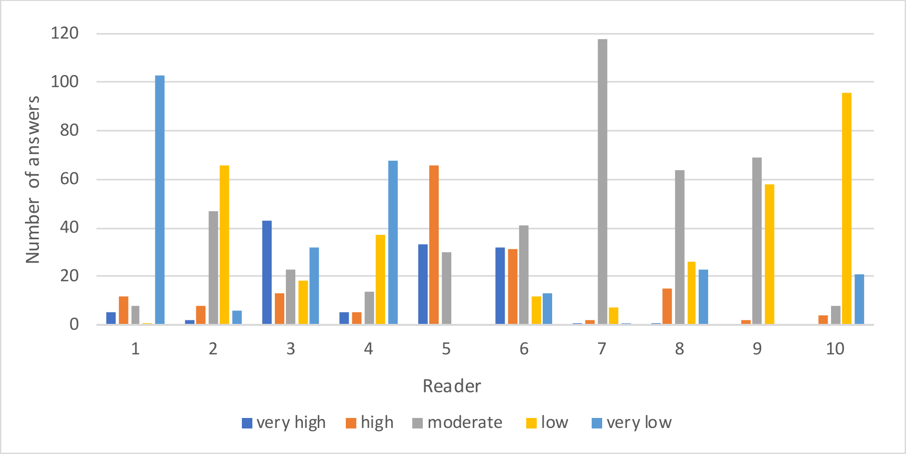

Fig. 3. Histograms of reader Likert-scale ratings for probability of perfusion deficit present.

Table 2
Receiver-operator characteristics (ROC) area under the curve (AUC) for specific readers.

Reader experience	Reader	Area	Std. Error	Asymptotic 95% CI	
				Lower Bound	Upper Bound
Beginner	Reader 1	0.504	0.051	0.403	0.604
	Reader 2	0.581	0.050	0.482	0.680
	Reader 3	0.625	0.049	0.529	0.722
	Reader 4	0.586	0.050	0.488	0.684
Intermediate	Reader 5	0.446	0.051	0.346	0.545
	Reader 6	0.601	0.050	0.504	0.699
Expert	Reader 7	0.555	0.051	0.456	0.655
	Reader 8	0.612	0.050	0.513	0.710
	Reader 9	0.524	0.051	0.424	0.624
	Reader 10	0.608	0.050	0.510	0.705

that dynamic myocardial CT perfusion brings incremental diagnostic value in addition to that obtained with CTCA alone, with 0.84 specificity and sensitivity 0.59 for diagnosis of ischemia [5]. Moreover, in patients with severe coronary calcification the combination of coronary CTA with dynamic CTP has better diagnostic accuracy than either coronary CTA or dynamic CTP alone [14]. Several reasons could be provide to explain these results.

First, these data are consistent with the evidence that diagnostic performance of functional-only approach in the setting of known obstructive disease is limited also for other second-line non-invasive imaging techniques is limited. Indeed, in Dan-NICAD study [15], 292 patients were randomized to stress CMR or to SPECT after initial CTCA that showed obstructive CAD. This study showed a sensitivity and specificity of 27%, 91% and 30%, 79% for single-photon emission computed tomography (SPECT) [15] and stress cardiac magnetic resonance (stress-CMR) [16], respectively. Differently from SPECT or CMR, dynamic CTP showed higher sensitivity and lower specificity due to its intrinsic higher spatial resolution.

Second, the reference included invasive FFR but not IMR. Therefore, there is a potential risk to lose microvascular disease and to wrongly classify some positive CTP as false positive case. This could be even more relevant considering that we have classified the patients according to absolute MBF rather than according to myocardial perfusion reserve due to the lack of data of rest perfusion.

Finally, in the previous reports the definition of positive stress CTP was based on the combination of obstructive CAD at CCTA with matched positive stress CTP. Therefore all cases with pathologic MBF in absence of obstructive CAD were graded as negative stress CTP with improvement of specificity and positive predictive value.

However, several strengths of the study should be considered. They include different reading environments from two major research hospitals (different processing workstations, different readers), and two groups of differently trained people with two specialties: radiologists and cardiologists, which may have had an influence on reading conditions. In this study, the readers could indicate the presence or absence of a perfusion defect with overall good sensitivity (0.79) but very poor specificity (0.21).

MBF values differ across patients and display large discrepancies in standard deviation, especially in segment 17 in negative cases, and segment 9 in positive cases. This can indicate suboptimal cardiac wall segmentation in the apical and mid inferoseptal segments, regardless of the presence or absence of ischemia. These discrepancies may be caused by the diaphragm movements, although a motion compensation algorithm has been applied to all cases.

The study has potential limitations. First, all datasets were prepared and post-processed by one study investigator. The dynamic study images were obtained at the GE scanner, then postprocessed at the Vitrea workstation and the perfusion slices and the perfusion maps were obtained from CardIQ workstation. These three types of images from could have introduced a potential diagnostic bias.

Second, the windowing of the images that could not be adjusted during the study may be another limitation. The readers were given prepared datasets, which could have also affected the quality of the readings as they could not scroll through or zoom in the datasets. Third, the readers also mentioned a substantial number of moving artifacts in the study datasets. These artifacts could not be quantified, even after the study, because their overlaying was too complex. Unfortunately, there is no quantifiable method to separate moving artifacts from beam hardening artifacts, especially on moving dynamic CTP images.

Table 3
Case-based sensitivity and specificity of dynamic CT perfusion for detection of perfusion deficit.

	Reader1	Reader 2	Reader 3	Reader 4	Reader 5	Reader 6	Reader 7	Reader 8	Reader 9	Reader 10	ALL
	Beginner				Intermediate		Experts				
sensitivity	0.85	0.80	0.53	0.95	0.70	0.97	0.78	0.40	0.95	0.98	**0.79**
specificity	0.24	0.21	0.65	0.16	0.43	0.06	0.35	0.75	0.09	0.04	**0.30**

Table 4
Mean MBF values per segment in all, negative and positive cases.

All cases																	
segment	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
average value	278.9	284.4	249.9	260.6	232.8	247.3	234.0	244.3	407.4	217.8	192.5	205.6	224.9	263.2	228.8	215.4	557.4
standard deviation	85.5	97.3	83.7	79.6	134.1	92.4	73.2	86.1	1931.6	70.3	65.6	68.6	68.4	101.1	84.5	187.3	3464.9
Positive cases																	
average value	259.4	273.3	236.4	240.8	205.6	236.4	217.4	228.6	529.8	200.8	184.2	197.2	208.7	241.2	216.9	217.6	229.0
standard deviation	82.3	95.6	83.8	73.6	89.4	90.2	71.3	92.2	2627.8	66.0	69.9	70.3	71.4	112.6	84.3	246.2	82.4
Negative cases																	
average value	301.4	297.1	265.4	283.5	264.0	259.8	253.2	262.2	266.6	237.4	202.0	215.3	243.6	288.4	242.6	212.8	934.9
standard deviation	83.5	97.8	80.7	80.2	166.3	93.2	70.6	74.6	208.0	70.0	59.0	65.4	59.5	78.8	82.7	75.5	5053.5

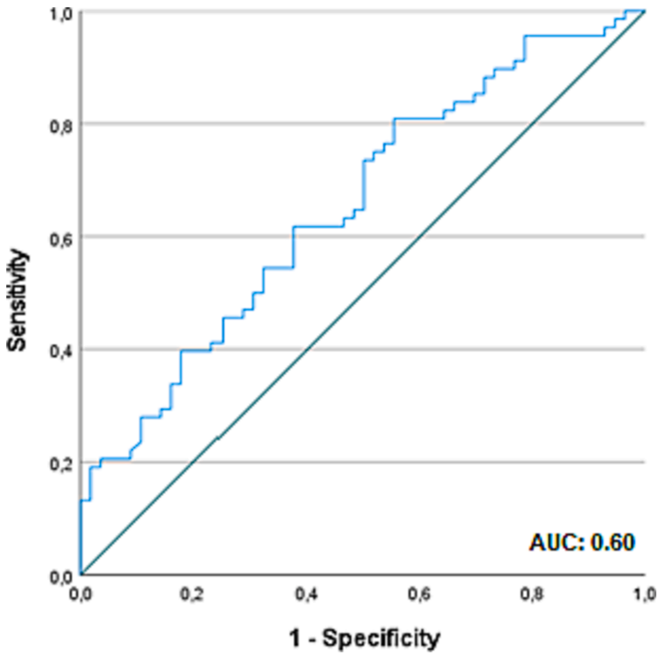

Fig. 4a. MBF diagnostic value for diagnosis of ischemia. ROC curve constructed from the lowest MBF value from the perfusion map. AUC = 0.60.

The provided perfusion maps can be a factor affecting diagnostic performance. The perfusion maps shown to the readers had a fixed scale from 0 to 150 ml/100 g/min, without the chance to perform a point-by-point MBF assessment. For this reason, readers could be deceived in detecting ischaemia in cases of mild MBF reduction, (i.e. 80–100 ml/100 g/min). However, this layout has been chosen as a preset delivered by the vendor, and not changed in order to let all the readers across the two different sites evaluate the same exact images.

5. Conclusions

This study suggests that stress-only dynamic CTP alone, without integration with CCTA data and rest CTP, does not provide enough diagnostic information to diagnose ischemia in patients with clinical indication for ICA and invasive FFR. Therefore, the true advantage of CTP may be the integration with coronary CTA. Further research is needed to facilitate clinical applicability and the development of a dynamic CTP one-stop-shop for ischemia diagnosis.

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CRediT authorship contribution statement

Olga Sliwicka: Writing – original draft, Investigation, Formal analysis, Conceptualization. **Andrea Baggiano:** Writing – review & editing, Methodology. **Ioannis Sechopoulos:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Gianluca Pontone:** Writing – review & editing, Supervision, Methodology.

Declaration of Competing Interest

Ioannis Sechopoulos has research agreements with Siemens Healthcare, Canon Medical Systems, ScreenPoint Medical, Sectra Benelux, Hologic, Volpara Healthcare, Lunit, iCAD, a speaker agreement with Siemens Healthcare, and is a Scientific Advisory Board member of

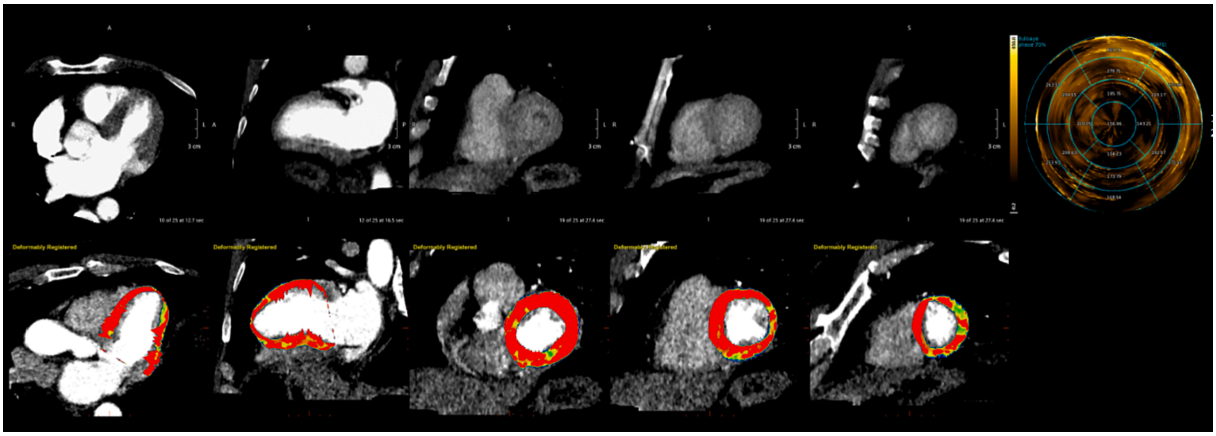

Fig. 4b. A study example case. 52-year-old patient with positive invasive FFR. Two out of ten readers correctly indicated presence of ischemia (yellow-green). Upper row: raw 5 dynamic CTP images and a perfusion map. lower row: perfusion slices with color-coded map related to MBF calculation.

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References

[1] G. Pontone, A. Rossi, M. Guglielmo, M.R. Dweck, O. Gaemperli, K. Nieman, et al., Clinical applications of cardiac computed tomography: a consensus paper of the European Association of Cardiovascular Imaging-part II, Eur. Heart J. Cardiovasc. Imaging. 23 (4) (2022) e136–e161.

[2] H. Nishiyama, Y. Tanabe, T. Kido, A. Kurata, T. Uetani, T. Kido, et al., Incremental diagnostic value of whole-heart dynamic computed tomography perfusion imaging for detecting obstructive coronary artery disease, J. Cardiol. 73 (5) (2019) 425–431.

[3] S.H. Kim, J. Rübenthaler, D. Nörenberg, T. Huber, W.G. Kunz, W.H. Sommer, et al., Cost-effectiveness of stress CTP versus CTA in detecting obstructive CAD or in-stent restenosis in stented patients, Eur. Radiol. 31 (3) (2021) 1443–1450.

[4] M. Lu, S. Wang, A. Sirajuddin, A.E. Arai, S. Zhao, Dynamic stress computed tomography myocardial perfusion for detecting myocardial ischemia: A systematic review and meta-analysis, Int. J. Cardiol. 258 (2018) 325–331.

[5] O. Sliwicka, I. Sechopoulos, A. Baggiano, G. Pontone, R. Nijveldt, J. Habets, Dynamic myocardial CT perfusion imaging-state of the art, Eur. Radiol. (2023).

[6] G. Pontone, A. Baggiano, D. Andreini, A.I. Guaricci, M. Guglielmo, G. Muscogiuri, et al., Stress computed tomography perfusion versus fractional flow reserve CT derived in suspected coronary artery disease: the PERFECTION study, JACC Cardiovasc. Imaging. 12 (8 Pt 1) (2019) 1487–1497.

[7] G. Pontone, A. Baggiano, D. Andreini, A.I. Guaricci, M. Guglielmo, G. Muscogiuri, et al., Dynamic stress computed tomography perfusion with a whole-heart coverage scanner in addition to coronary computed tomography angiography and fractional flow reserve computed tomography derived, JACC: Cardiovasc. Imaging. 12 (12) (2019) 2460–2471.

[8] K. Boedeker, AiCE Deep Learning Reconstruction: Bringing the power of Ultra-High Resolution CT to routine imaging, Canon Medical Systems Corporation. (2019) (MCACT0339EA 2019–01 CMSC).

[9] M. Akagi, Y. Nakamura, T. Higaki, K. Narita, Y. Honda, J. Zhou, et al., Deep learning reconstruction improves image quality of abdominal ultra-high-resolution CT, Eur. Radiol. 29 (11) (2019) 6163–6171.

[10] J.A. Johnson, T.A. Wilson, A model for capillary exchange, Am. J. Physiol. 210 (6) (1966) 1299–1303.

[11] A. So, J. Hsieh, J.Y. Li, J. Hadway, H.F. Kong, T.Y. Lee, Quantitative myocardial perfusion measurement using CT perfusion: a validation study in a porcine model of reperfused acute myocardial infarction, Int. J. Cardiovasc. Imaging. 28 (5) (2012) 1237–1248.

[12] T.K. Koo, M.Y. Li, A guideline of selecting and reporting intraclass correlation coefficients for reliability research, J. Chiropractic Med. 15 (2) (2016) 155–163.

[13] D. Cicchetti, Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology, Psychol. Assessment. 6 (1994) 284–290.

[14] T.A. Magalhaes, S. Kishi, R.T. George, A. Arbab-Zadeh, A.L. Vavere, C. Cox, et al., Combined coronary angiography and myocardial perfusion by computed tomography in the identification of flow-limiting stenosis - The CORE320 study: An integrated analysis of CT coronary angiography and myocardial perfusion, J. Cardiovasc. Comput. Tomogr. 9 (5) (2015) 438–445.

[15] L. Nissen, S. Winther, J. Westra, J.A. Ejlersen, C. Isaksen, A. Rossi, et al., Diagnosing coronary artery disease after a positive coronary computed tomography angiography: the Dan-NICAD open label, parallel, head to head, randomized controlled diagnostic accuracy trial of cardiovascular magnetic resonance and myocardial perfusion scintigraphy, Eur. Heart J. Cardiovasc. Imaging. 19 (4) (2018) 369–377.

[16] L.D. Rasmussen, S. Winther, A. Eftekhari, S.R. Karim, J. Westra, C. Isaksen, et al., Second-line myocardial perfusion imaging to detect obstructive stenosis: head-to-head comparison of CMR and PET, JACC Cardiovasc. Imaging. 16 (5) (2023) 642–655.