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## Research article

# Non-invasive fractional flow reserve (FFR<sub>CT</sub>) in the evaluation of acute chest pain – Concepts and first experiences

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## ABSTRACT

**Objective:** To evaluate 30 day rate of major adverse cardiac events (MACE) utilizing cCTA and FFR<sub>CT</sub> for evaluation of patients presenting to the Emergency Department (ED) with acute chest pain.

**Materials and methods:** Patients between the ages of 18–95 years who underwent clinically indicated cCTA and FFR<sub>CT</sub> in the evaluation of acute chest pain in the emergency department were retrospectively evaluated for 30 day MACE, repeat presentation/admission for chest pain, revascularization, and additional testing.

**Results:** A total of 59 patients underwent CCTA and subsequent FFR<sub>CT</sub> for the evaluation of acute chest pain in the ED over the enrollment period. 32 out of 59 patients (54 %) had negative FFR<sub>CT</sub> (>0.80) out of whom 18 patients (55 %) were discharged from the ED. Out of the 32 patients without functionally significant CAD by FFR<sub>CT</sub>, 32 patients (100 %) underwent no revascularization and 32 patients (100 %) had no MACE at the 30-day follow-up period.

**Conclusion:** In this limited retrospective study, patients presenting to the ED with acute chest pain and with CCTA with subsequent FFR<sub>CT</sub> of >0.8 had no MACE at 30 days; however, for many of these patients results were not available at time of clinical decision making by the ED physician.

## 1. Introduction

Coronary computed tomography angiography (cCTA) has become both an established and a frequently utilized imaging modality for the assessment of coronary artery disease (CAD). The high negative predictive value makes this an ideal diagnostic modality for the assessment of symptomatic patients with low to intermediate pre-test probability [1]. However, this test shares relatively poor specificity in relation to lesion specific ischemia with other mere morphologic modalities, such as invasive catheter angiography (ICA) [2,3]. To overcome this limitation, fractional flow reserve (FFR) can be used as an adjunct to ICA [4],

which allows for hemodynamic assessment of lesion specific ischemia, overcoming the limitation seen with visual stenosis assessment alone [5]. Data have demonstrated improved patient outcomes and improved survival when FFR it utilized to guide revascularization [6,7].

Integrating computational fluid dynamics and advanced 3-D image modeling allows for the noninvasive calculation of FFR utilizing standard cCTA datasets [8–10]. This cCTA derived FFR (FFR<sub>CT</sub>) has been validated in several clinical trials which have shown good correlation with invasive FFR [11–13]. Additionally, other data demonstrate improved time to diagnosis and cost effectiveness while maintaining safety utilizing a FFR<sub>CT</sub> guided approach for the evaluation of coronary

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artery disease (CAD) [14–16]. The patients in these trials were largely outpatients referred for non-emergent ICA who had undergone prior cCTA without an intervening coronary event [11–13]. Subsequently, there exists a paucity of data for the use of FFR<sub>CT</sub> in the evaluation of patients presenting with acute chest pain. As more than 6 million patients present with acute chest pain annually to Emergency Departments (ED) across the United States, acute chest pain represents an important health problem [17–19].

The purpose of this study therefore was to evaluate 30 day event rates in patients who presented to our institution's ED with acute chest pain who underwent evaluation with cCTA and subsequent FFR<sub>CT</sub>.

## 2. Materials and methods

### 2.1. Patient population

Patients between the ages of 18–95 years of age who presented to the ED with a chief complaint of chest pain, which was deemed to be of possible cardiac etiology by treating ED physician, and underwent evaluation with clinically indicated cCTA and subsequent FFR<sub>CT</sub> were eligible for inclusion in the study. This retrospective study was approved through the institution's IRB with a waiver of consent. The cohort comprises the initial group of consecutive patients who met the inclusion criteria between July 22, 2018 and April 28, 2019, immediately after we opened up the use of FFR<sub>CT</sub> to the acute chest pain population. At our institution, cCTA for acute chest pain is available on a 24/7 basis. Patients presenting with ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), or hemodynamic instability are clinically excluded from CT scanning. For study purposes, patients were excluded if they had a known history of myocardial infarction or prior cardiac intervention (coronary artery bypass surgery or percutaneous coronary intervention), or structural variations (anomalous coronary artery). Additionally, patients were excluded for insufficient cCTA image quality (poor vessel opacification, presence of motion artifact, etc., rendering the imaging study unsuitable for CT-FFR analysis. Demographic and outcomes data were obtained through review of the patients electronic medical record (EMR). Treatment decisions such as admission or discharge from the ED and what if any follow up testing was performed were at the discretion of the treating physicians.

### 2.2. Cardiac computed tomography angiography and FFR<sub>CT</sub> analysis

cCTA was performed using a 2nd or 3rd generation dual-source CT (DSCT) systems (Somatom Definition Flash, Somatom Definition Force Siemens Healthineers, Forchheim, Germany) preceded by a non-contrast calcium scoring study. For the subsequent contrast-enhanced coronary CTA, scan parameters consisted in tube voltage of 100–120 kV and tube current of 320–412 mA. Contrast enhancement was achieved by injecting 50–80 mL iopromide (Ultravist 370mgI/mL, Bayer, Wayne, NJ) at 4–6 mL/s followed by a 30 mL saline bolus chaser. Beta-blockers and nitroglycerine were used if necessary at the discretion of the attending physician. Image reconstruction was performed at the optimal cardiac phase with a section thickness of 0.75 mm, a reconstruction increment of 0.5 mm, and a smooth convolution kernel.

After the preliminary clinical interpretation by our residents, cCTA datasets were re-analyzed by experienced, board-certified readers who issued the final report. Image analysis used transverse sections and automatically generated curved multiplanar reformatted views. Qualitative angiographic analysis was performed on all patients adhering to the Coronary Artery Disease-Reporting and Data System (CAD-RADs) guidelines. Patients were categorized, by an experienced cardiovascular radiologist, according to maximal coronary stenosis and assigned as having no stenosis (0 %), mild (1–49 %), moderate (50–69 %), severe (70–99 %), and occluded (100 %) [20].

FFR<sub>CT</sub> analysis using computational fluid dynamics was performed

offsite via HeartFlow® (Redwood City, CA). After review of cCTA images by a cardiovascular radiologist, data sets were transferred for off-site analysis if there was stenosis in any major epicardial coronary artery of >30 % but <90 %. A FFR<sub>CT</sub> value of ≤0.8 was considered diagnostic for hemodynamic significance of the stenosis in question. In the case of focal lesions the FFR<sub>CT</sub> value was adjudicated distal to the stenosis. FFR<sub>CT</sub> values were adjudicated utilizing the lowest value in the setting of sequential stenoses.

### 2.3. Follow up

Follow up was conducted through review of the patient's EMR. Demographic data was captured through review of documentation in the EMR at the time of the index encounter. Follow up data was obtained through review of the patient's EMR capturing all subsequent encounters at our institution up to 30 days after the index ED encounter. The primary endpoint of the study was 30 day rate of major adverse cardiac event (MACE) defined as death from cardiovascular cause, myocardial infarction (MI), unstable angina, and revascularization not prompted by the imaging study. Additionally, we captured the rate of readmission and repeat evaluation for chest pain in the Emergency Department.

### 2.4. Statistical methods

Continuous variables are represented as mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on their distribution (tested with Shapiro Wilks test). Categorical data is displayed as absolute frequencies and proportions. Sensitivity, specificity, negative predictive value, and positive predictive value were analyzed using electronic medical record data for adjudication of MACE.

## 3. Results

### 3.1. Patient population

The final patient population included 59 patients (54 % male, 66 % Caucasian) with a mean age of 64.5 ± 10.6 yrs. Patients demonstrated typical risk factors for CAD with 53 % having a history of smoking, 71 % a history of hypertension, 31 % were diabetics, and 61 % had a history of dyslipidemia.

### 3.2. Coronary computed tomography angiography and FFR<sub>CT</sub> results

Of the patients included in the final analysis 3 (5 %), 8 (14 %), 29 (49 %), and 19 (32 %) had no, mild, moderate, and severe stenosis via qualitative assessment respectively. A total of 32 (54 %) had a FFR<sub>CT</sub> value >0.80 indicating the absence of lesion specific ischemia; while 27 (46 %) had a value ≤0.8 indicating obstructive CAD. No patients qualitatively assigned as having no or mild stenosis had a FFR<sub>CT</sub> value ≤0.80. Of the patients with moderate stenosis, 31 % (9 of 29) and of those with severe stenosis, 89 % (17 of 19), had FFR<sub>CT</sub> values ≤0.80. Qualitative angiographic and FFR<sub>CT</sub> data are provided in Table 1. Breakdown of FFR<sub>CT</sub> values provided in Table 2. The average turnaround time for obtaining FFR<sub>CT</sub> results was 3.5 h (range 1.4 h–14.7 h). This represents the time to obtain results from when the data was sent to HeartFlow for further analysis. Data was sent for FFR<sub>CT</sub> analysis only after initial ED physician evaluation, obtaining CCTA, and initial CCTA review by the cardiovascular radiologist. Clinical decisions, in many cases appeared to be made prior to obtaining the results of the FFR<sub>CT</sub> analysis. While, unable to determine the exact number of cases this occurred in, it is estimated to be possible in up to approximately 30 % of cases (based on estimation from length of stay in the ED when compared to time to results of FFR<sub>CT</sub> analysis).

**Table 1**

Procedural results of the per patient analysis. Total patient cohort (n = 59).

Coronary CT angiography	
CAD-RADS™ classification	
CAD-RADS™ 0	3 (5 %)
CAD-RADS™ 1 + 2	8 (14 %)
CAD-RADS™ 3	29 (49 %)
CAD-RADS™ 4	19 (32 %)
Coronary CT angiography-derived fractional flow reserve (FFR <sub>CT</sub> )	
FFR <sub>CT</sub> ≤0.80	27
CAD-RADS™ 0 and FFR <sub>CT</sub> ≤0.80	0
CAD-RADS™ 1 + 2 and FFR <sub>CT</sub> ≤0.80	0
CAD-RADS™ 3 and FFR <sub>CT</sub> ≤0.80	9 (33 %)
CAD-RADS™ 4 and FFR <sub>CT</sub> ≤0.80	18 (67 %)

Data are presented as numbers with percentages (%). CAD-RADS™ = coronary artery disease reporting and data system, FFR<sub>CT</sub> = coronary computed tomography angiography-derived fractional flow reserve.

**Table 2**FFR<sub>CT</sub> values as a continuous variable for total patient cohort (n = 59).

FFR <sub>CT</sub> Values	Number of Patients
≥ 0.9	6
0.85 – 0.89	12
0.8 – 0.84	14
0.75 – 0.79	7
0.7 – 0.74	5
0.6 – 0.69	7
< 0.6	8

### 3.3. Follow up testing

Subsequent to obtaining cCTA and FFR<sub>CT</sub> results, 6 patients underwent immediate referral for follow up stress testing utilizing single-photon emission computed tomography (SPECT) in 5 patients, stress cardiac magnetic resonance imaging (CMRI) in 1 patient, and 19 underwent ICA. Decisions for subsequent testing, including proceeding to ICA, were at the discretion of the treating cardiologist, without defined criteria. Four of the 6 patients who underwent follow up SPECT and the stress CMRI had FFR<sub>CT</sub> values >0.80. Of these patients 100 % were found to have normal myocardial perfusion without evidence of ischemia. Of the 19 patients who underwent ICA, 16 (84 %) had FFR<sub>CT</sub> values ≤0.80. Of the 16 patients with FFR<sub>CT</sub> ≤0.80 who underwent ICA, 9 (56 %) had obstructive disease angiographically, of which 7 underwent revascularization. Of the remaining 2 patients who did not undergo revascularization, one was deemed to have non-revascularizable disease by the treating invasive cardiologist and the other died prior to undergoing recommended CABG. Of the 3 patients who underwent ICA and had FFR<sub>CT</sub> values >0.80; all 3 patients were found to have non-obstructive disease. Three patients whom underwent ICA also received invasive FFR at that time. Invasive FFR and FFR<sub>CT</sub> results were congruent in 1 case with FFR<sub>CT</sub> demonstrating non-obstructive disease with a value of 0.85 which was confirmed non-obstructive with invasive FFR with a value of 1. In 2 cases the results were divergent with FFR<sub>CT</sub> values of 0.69 and 0.5 which were deemed non-obstructive via invasive FFR with results of 0.92 and 0.88 respectively.

### 3.4. Clinical outcomes

Of the 59 patients who underwent cCTA and subsequent FFR<sub>CT</sub> in the ED for evaluation of chest pain, 25 (42 %) were discharged to home from the ED and 34 (58 %) were admitted for further evaluation. Of the 25 patients who were discharged from the ED, 18 had FFR<sub>CT</sub> values >0.8. Of these 18 patients, who were discharged from the ED with no FFR<sub>CT</sub> values ≤0.8, there were 0 MACE at the end of the 30 day follow up period.

There was one patient who was readmitted for recurrent chest pain and underwent ICA within 30 days. ICA revealed non-obstructive CAD and no revascularization was performed. Within the group of 7 patients who were discharged from the ED with FFR<sub>CT</sub> ≤0.8 there were 2 MACE occurring in the same patient (death in setting of elevated cardiac biomarkers) during the 30 day follow up period. It should be noted that in this case the patient was discharged from the ED prior to obtaining the FFR<sub>CT</sub> data and represented within 24 h. An additional patient was readmitted within 30 days for recurrent chest pain. During that re-admission ICA was recommended but refused by the patient. Rates of 30 day MI, death, and revascularization for all patients discharged from the ED with a FFR<sub>CT</sub> >0.8 were 0%. Please see Fig. 1 for results of patient outcomes stratified by FFR<sub>CT</sub> results. Representative case with CT angiography and patient specific FFR<sub>CT</sub> analysis presented in Fig. 2.

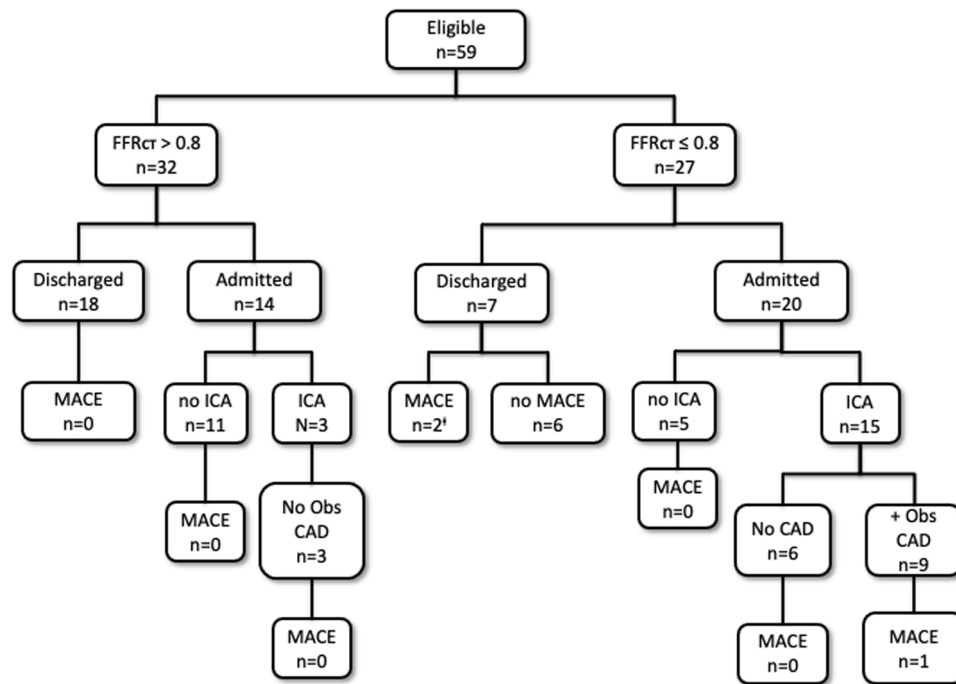
Of the 34 patients who were admitted to the hospital, 14 had FFR<sub>CT</sub> >0.8. Eleven of these 14 patients underwent no further ischemic evaluation as an inpatient and, following discharge, had no MACE during the follow up period. The remaining 3 patients underwent ICA that demonstrated no obstructive CAD and underwent no revascularization.

Out of the entire cohort of 59 patients, a total of 32 patients had FFR<sub>CT</sub> analysis that did not demonstrate lesion specific ischemia and had no FFR<sub>CT</sub> values of ≤0.80. Within this group there were no incidents of revascularization nor MACE at the 30 day follow up period. Additionally, of the 5 patients with FFR<sub>CT</sub> >0.8 who underwent additional non-invasive functional testing (SPECT and stress CMR) non were found to have findings suggestive of ischemia. Of the 3 patients whom underwent ICA with FFR<sub>CT</sub> >0.8 none were found to have obstructive disease. There was one 30-day readmission in this group for recurrent chest pain, at which point ICA was performed and noted to have non-obstructive disease as describe above. Overall, a negative FFR<sub>CT</sub> in the setting of acute chest pain translates into a high negative predictive value of 100 % to exclude 30 day MACE in this preliminary cohort.

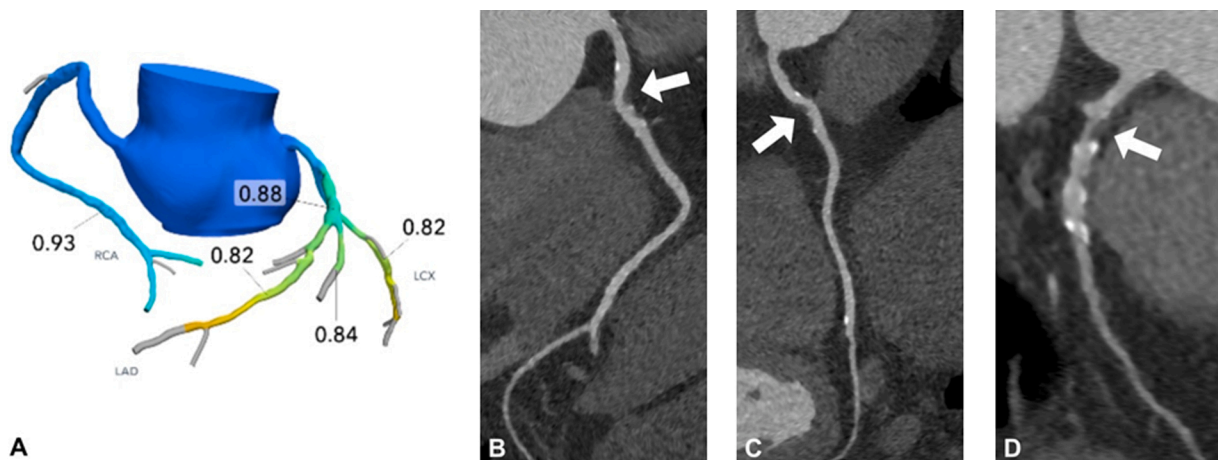
## 4. Discussion

Our study demonstrates the potential utility for use of cCTA and subsequent FFR<sub>CT</sub> for evaluation of obstructive CAD in patients presenting with acute chest pain in an ED setting. While prior studies have demonstrated the utility of cCTA-derived FFR<sub>CT</sub> in the stable chest pain population [11–13,21], the use of this approach in the acute setting is only beginning to be studied. Our data suggest that FFR<sub>CT</sub> could be utilized to risk stratify patients who present to the ED with acute chest pain helping to differentiate those who would benefit from admission and further invasive management versus those who could be safely discharged.

Previous investigations have demonstrated that use of cCTA in the evaluation of acute chest pain in the ED can lead to shorter time to diagnosis, faster ED disposition times and even lower cost of care when compared to SPECT [22,23]. Moreover, there were no differences between the two modalities in regards to MACE during 6 month follow up [23]. Additional studies comparing the full range of options available to an ED physician, not just SPECT, demonstrated that use of cCTA resulted in a shorter length of stay without jeopardizing safety [24]. However, several of these investigations also demonstrated an increase in downstream testing, including additional functional testing and ICA in the cCTA groups [22,24]. This mirrors the findings of larger studies utilizing cCTA in the evaluation of stable chest pain, which demonstrate an increase in the use of ICA subsequent to cCTA [25]. The etiology of this is likely related to the relatively poor specificity of a stand-alone anatomic assessment when compared to invasive hemodynamic assessment [2], as well as the direct visualization of atherosclerotic disease by cCTA, obstructive or not, triggering ICA referral. Similarly, our study demonstrated that 48 (81 %) patients had at least moderate stenosis on anatomical cCTA assessment, yet only 27 (46 %) had functionally significant disease via FFR<sub>CT</sub> assessment. It is in this discrepancy that FFR<sub>CT</sub> demonstrates its utility. The use of FFR<sub>CT</sub> has been shown to improve the



**Fig. 1.** Flowchart showing patient outcomes stratified by FFR<sub>CT</sub> results. MACE – Major Adverse Cardiac Events, ICA – Invasive Coronary Angiography, Obs CAD – Obstructive Coronary Artery Disease. † There were 2 events in one patient who died in the setting of elevated cardiac biomarkers.



**Fig. 2.** 72-year-old man with acute chest pain presenting to the ED. cCTA with moderate stenosis in the RCA (B, C) and proximal LAD (D). Negative FFR<sub>CT</sub> (A) enabled discharge from ED without 30 day MACE.

specificity of cCTA [13] and thus may help to reduce referrals to ICA in patients without functionally significant disease. Indeed, Lu et al. were able to demonstrate this using an observational cohort of patients from the PROspective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) Trial. By only proceeding to ICA in those patients with CAD on cCTA with a FFR<sub>CT</sub> value of ≤0.8, the rate of ICA demonstrating <50 % stenosis could be reduced by 44 % [14]. Additionally, the rate of ICA resulting in revascularization increased by 24 % [14]. This is similar to results of the “Propective Longitudinal Trial Of FFR<sub>CT</sub>: Outcome and Resource iMpaCts” study (PLATFORM) trial which demonstrated a reduction in the number of ICAs in patients with non-obstructive disease when a cCTA/FFR<sub>CT</sub> strategy was utilized [16]. These results were also demonstrated by Fairbairn et al. in the Assessing Diagnostic Value of Non-invasive FFR<sub>CT</sub> in Coronary Care (ADVANCE) registry, which included more than 5000 patients, with findings of non-obstructive CAD

at the time of ICA of 14 % in patients with FFR<sub>CT</sub> values of ≤0.8, compared to 43.8 % in patients with values >0.8 [26]. Similarly, in our study 32 patients had FFR<sub>CT</sub> values >0.8. Of these, 7 (22 %) underwent additional testing, all of whom demonstrated no evidence of functionally significant disease on ICA, SPECT, or stress CMRI. Additionally, 14 patients with FFR<sub>CT</sub> values of >0.8 were admitted to the hospital and underwent no revascularization and had no MACE during the follow up period. These patients could have been safely discharged home from the ED, effectively reducing the admission rate by 41 % along with avoiding trickle-down follow-up testing, including the avoidance of subsequent SPECT. Interestingly, more than half of the patients referred for subsequent SPECT in our study had no ischemic causing lesions via FFR<sub>CT</sub>. As these patients were presenting for evaluation for acute chest pain, the focus, from a diagnostic strategy, would be the exclusion of obstructive CAD. As Driessen et al. demonstrated, FFR<sub>CT</sub> possess a higher sensitivity



on both a per vessel and per patient level than SPECT (90 % vs 42 % and 96 % vs 61 % respectively) [27]. These data suggest SPECT is a poor follow up test to an already negative FFR<sub>CT</sub> result.

The safety of deferring further evaluation on the basis of non-obstructive FFR<sub>CT</sub> values has been previously demonstrated in the PLATFORM data [15,16]. At 90-day follow-up, patients who were to undergo initial invasive management but assigned to the cCTA-FFR<sub>CT</sub> arm had a 1% rate of MACE (2/193) [16]. In one of the cases urgent revascularization was performed after the cCTA and FFR<sub>CT</sub> demonstrated severe disease. A second case included a peri-procedural myocardial infarction in a patient whose cCTA was of insufficient quality to allow for FFR<sub>CT</sub> analysis. There were no adverse events noted in the 61 % of patients whose ICA was cancelled based of negative cCTA/FFR<sub>CT</sub> results [16]. Additionally, within this same cohort of patients, when follow-up was extended to 1 year, there were no MACE [15]. Again these results were similar to the ADVANCE registry with no MACE noted during a 90 day follow up period in patients with FFR<sub>CT</sub> >0.8 [26].

It is again worth noting that the aforementioned data included only clinically stable outpatients. The use of a CCTA/FFR<sub>CT</sub> strategy in the setting of acute chest pain has not been as extensively studied. Recently, the first study evaluating the use of FFR<sub>CT</sub> within the acute chest pain population was published. Chinnaiyan et al. compared a strategy of CCTA alone vs CCTA + FFR<sub>CT</sub> in patients presenting to the ED with acute chest pain [28]. A total of 555 patients were included in the cohort with 297 patients undergoing CCTA + FFR<sub>CT</sub> and 258 patients undergoing CCTA only [28]. Within the group undergoing CCTA + FFR<sub>CT</sub>, the rate of MACE at 90 day follow was low at 2.7 % [28]. Additionally, in patients with a negative FFR<sub>CT</sub> whom ICA was deferred, there were no deaths or myocardial infarctions observed [28]. Similar to previously mentioned studies, rates of ICA resulting in the diagnosis of non-obstructive CAD were significantly reduced in the FFR<sub>CT</sub> group compared to CCTA alone (8% vs 56.5 %) [28]. These results are in line with our findings which demonstrated that in patients with FFR<sub>CT</sub> values >0.8, 100 % had no MACE at 30 day follow up. Additionally, within our cohort of patients with FFR<sub>CT</sub> >0.8 who underwent further testing with ICA, 100 % demonstrated findings of non-obstructive CAD.

Our study has several limitations. First, this represents a small, real-life single center experience that included only 59 patients. Larger multi-site trials will be needed to further evaluate the feasibility and safety for use of FFR<sub>CT</sub> in the evaluation of acute chest pain in the ED setting. Additionally, while the final patient population evaluated was 59 patients, several studies were excluded because of insufficient image quality that did not allow for FFR<sub>CT</sub> analysis. Since FFR<sub>CT</sub> has become available at our institution, successful analysis has occurred in 76 % of patients. One possible explanation for the rate of rejection in this study could be related to the less controlled setting in the ED compared to the elective evaluation of outpatients. In this scenario patients are often in pain and acute distress, and when combined with less rigorous use of both beta-blockers and nitrates prior to cCTA during off-hours, may result in increased motion artifacts and decreased image quality precluding FFR<sub>CT</sub> analysis. Additionally, not only was the prevalence of disease within our patient population high, so too was the disease severity. Only 3 patients were deemed to be completely free of atherosclerosis (i.e., CAD-RADS 0), while 81 % of patients had >50 % stenosis on qualitative assessment. This high disease prevalence may have resulted in selection bias. Moreover, in patients whom underwent ICA, invasive FFR measurements were obtained in only 3 patients. Invasive FFR was congruent with FFR<sub>CT</sub> in only 1 case. On the surface this raises concern; however, the numbers are too small to draw any meaningful conclusion. Inclusion of routine invasive FFR measurements in future studies of the use of FFR<sub>CT</sub> in this patient population is needed. Perhaps most importantly, our analysis describes our very initial experience with making FFR<sub>CT</sub> available for ED patients presenting with acute chest pain. The results most certainly reflect a degree of variable familiarity of ED physicians with this test and resulting inhomogeneity in their

processing, use, and subsequent management decisions relative to FFR<sub>CT</sub> results. As such clinical decision making without utilization of FFR<sub>CT</sub> results may have taken several forms including: pre-emptive decision making prior to obtaining FFR<sub>CT</sub> results, lack of clarity as to how to interpret and utilize FFR<sub>CT</sub> analysis, or even disregard as to FFR<sub>CT</sub> results. To this point 14 patients with a FFR<sub>CT</sub> value of >0.8 were still admitted to the inpatient cardiology teams. This may have been related to variable familiarity as described above or utilization of other risk stratification tools for which the ED providers are more familiar with. One such tool is the HEART score which is a risk stratification tool utilizing a scoring system of both subjective (description of symptoms) and objective (age, presence of risk factors, etc) to predict patients at high risk of MACE in the next 30 days. Given the overall high burden of disease and comorbidities within our patient population it would be expected that most patients would have yielded elevated HEART scores. Thus treating ED physicians may have been more likely to base decisions on a more conservative and familiar scoring system than utilize a newer technology. Similarly, there was inhomogeneity in the decision to proceed with further evaluation with ICA. To this point 3 patients with FFR<sub>CT</sub> values of >0.8 underwent ICA. Similar to decisions made about admission vs discharge this may have represented a degree of unfamiliarity with FFR<sub>CT</sub> by the treating cardiologist and a reluctance to rely on data from a new technology in the face of a qualitative stenosis assessment of at least moderate stenosis in a patient reporting chest pain. Additionally, in one patient with FFR<sub>CT</sub> >0.8, ICA was not performed at the index hospitalization but was performed when the patient represented within 30 days with recurrent chest pain. We anticipate that increased education and systems based approaches targeting more standardization of practice will result in a more homogenous, algorithmic approach to the integration of FFR<sub>CT</sub> with clinical findings and other test results. Given the retrospective nature of the study design, adjudication of MACE was performed utilizing data from the electronic medical record at our facility. As such we are unable to exclude MACE that could have occurred at another facility. A prospective design, where patient follow up is performed, is currently underway and would help to ensure more accurate MACE adjudication. Finally, in a number of cases patient management decisions were arguably made before FFR<sub>CT</sub> results became available. A further reduction in analysis time will likely enhance the integration of FFR<sub>CT</sub> data in patient disposition in the fast-paced ED environment.

## 5. Conclusion

In this limited retrospective study, patients presenting to the ED with acute chest pain and with CCTA with subsequent FFR<sub>CT</sub> of >0.8 had no MACE at 30 days; however, for many of these patients results were not available at time of clinical decision making by the ED physician.

## CRedit authorship contribution statement

All authors contributed significantly to this submission as well as to the revision that we are now submitting. Further breakdown can be provided if requested as being necessary.

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