Exploring diastolic pressure ratio to fractional flow reserve discordance and a hypothesis on tailoring diastolic pressure ratio cut-off values to improve diagnostic accuracy in the mid- and distal-LAD

C. Balfe [a,1,*], B. Jacob [b,1], N. Hickey [a,1], D. Moore [a,1], D. Mulcahy [a,1], B. Loo [a,1]

[a] Tallaght University Hospital, Ireland
[b] Victoria Hospital, Kirkcaldy, United Kingdom

A B S T R A C T

Previous studies have identified a higher rate of discordance between non-hyperaemic pressure ratios and FFR in the LAD when compared to the other two coronary arteries. We hypothesised that in keeping with recently published data, we would identify a higher discordance rate between diastolic pressure ratio (DPR) and FFR in the LAD compared to the RCA or LCx. In our study, 12.7% of LAD lesions had discordant results compared with 2.4% of non-LAD lesions. This represents a statistically significant increased rate of discordance in LAD lesions compared to non-LAD lesions (p = 0.04986). Note was made of a tendency for non-proximal LAD lesions to be associated with false-positive DPR results in the borderline range (0.88 and 0.89). In a speculative, hypothesis generating post-hoc analysis, we found an improved diagnostic accuracy of DPR when the cut-off value for a positive DPR in the non-proximal LAD was changed to ≤0.87. It is fathomable that improvements in the diagnostic accuracy of DPR for FFR may be improved by tailoring DPR cut-offs to the location of the lesion assessed.

1. Introduction

The non-hyperaemic pressure ratios (NHPRs) allow physiologic assessment of intermediate severity stenoses without the need for hyperaemic agents.

The first of the non-hyperaemic pressure indices, iFR, measures the mean ratio of distal coronary pressure to aortic pressure within the "wave-free period", beginning 25% of the way into diastole and ending 5 ms before the end of diastole.

Use of other intervals within the diastolic period have been demonstrated to produce numerically nearly identical results as iFR [1].

Discordance, as a result of a false negative or false positive iFR, ranges from 11.8% to 21.9% of cases in major published studies. Several associations with iFR to FFR discordance have been noted (Table 1) [2–9].

In the Long-Term Clinical Outcomes of NHPRs Study Lee et al. published data regarding the long-term clinical outcomes of non-hyperaemic pressure ratios. This group investigated the association between the NHPRs and the risk of a 5-year vessel oriented composite outcome (a composite of cardiac death, vessel-related myocardial infarction, and ischaemia driven revascularisation). The decision to revascularize in this study was based mainly off the FFR value. The cumulative incidence of the vessel-oriented composite outcome was lowest, at 7.5%, in patients in whom PCI was deferred due to a concordant negative NHPR and FFR.

Intriguingly, for those patients with discordant NHPR and FFR in whom PCI was deferred, the vessel oriented composite outcome was the same as for those patients who were revascularized (14.4% and 14.8%) [10].

The authors consider the implication that there may exist a risk continuum from concordant negative to concordant positive lesions, with discordant results representing a risk category in between these two poles. Accordingly, recommendation is made for discordant lesions to undergo meticulous follow-up with intensive secondary prevention.

Of interest is the finding in this study that discordant results were found most often in LAD lesions. In the per-vessel analysis, 12.9% of LAD lesions were discordant, compared to 5.43% of RCA lesions and 1.63% of LCx lesions. 64.9% of all discordant lesions occurred in the LAD, despite LAD lesions accounting for 33% of all lesions assessed.

* Corresponding author at: Tallaght University Hospital, Tallaght, Dublin 24 D24 NROA, Ireland.
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Table 1

Published evidence on discordance rates between iFR and FFR and the associations with discordance.

Published Evidence on Discordance between iFR and FFR	Discordance (%)	iFR cut-off
Jeremias et al. (2014) – RESOLVE	19.6	≤0.9
Escaned et al. (2015) – ADVISE II	17.5	≤0.89
Johnson et al. (2018)	20.1	≤0.9
Hennigan et al. (2016)	21	≤0.9
Cook et al. (2017)	14	≤0.89
Lee et al. (2017)	11.8	≤0.89
Dérimay et al. (2019)	20.6	≤0.89
Warisaw et al. (2019)	21.9	≤0.89
Lee et al. (2019)	13.3	≤0.89
Associations with Discordance	**iFR+/FFR−**	**iFR−/FFR+**
Hennigan et al. (2016)	Proximal lesions	Proximal lesions
Cook et al. (2017)	Diabetes mellitus	
Lee et al. (2017)	Female sex	
	Diabetes mellitus	
	Higher % stenosis	
	Smaller vessel diameter	
Dérimay et al. (2019)	Increased age	LMCA or proximal LAD stenosis
	Lower stenosis severity	Lower heart rate
	Lack of beta blocker use	
Warisaw et al. (2019)	More physiologically diffuse disease	More focal disease
Lee et al. (2019)	Diabetes mellitus	Greater diameter stenosis
	Acute coronary syndromes	

This finding of a higher rate of misclassification in the LAD contrasts with findings from the earlier RESOLVE study where no significant differences in diagnostic accuracy were noted when LAD coronary artery stenoses were compared with non-LAD coronary artery stenoses [2].

We sought to evaluate the per-vessel rate of discordance between the diastolic pressure ratio as compared to FFR in consecutive patients with intermediate severity coronary stenoses. The diastolic pressure ratio (DPR) uses the average Pd/Pa during the entire diastole. Like several other non-hyperaemic pressure indices, it is reported to produce numerically nearly identical results to iFR [1].

2. Methods

In this retrospective single centre study, DPR and FFR testing was carried out in intermediate severity coronary stenoses between March 2019 and January 2021. All patients who underwent physiological assessment with both DPR and FFR within the specified study period were included.

Before admission to the cardiac catheterization laboratory, patients had a large bore peripheral cannula inserted for administration of intravenous adenosine. Following diagnostic angiography, the OPSENS Optowire was flushed and inserted into the guiding catheter. Standard protocol was utilised.

Following administration of 200 μg of intracoronary isosorbide dinitrate the diastolic pressure ratio was measured. DPR was measured three times and an average taken. Then, intravenous infusion of adenosine at 140 mcg/kg/minute was administered until conditions of stable maximal hyperaemia were attained and the fractional flow reserve was documented. The adenosine infusion was then stopped, and the wire was slowly withdrawn into the catheter to assess for pressure drift.

Data were analysed on a per-patient basis for clinical characteristics and on a per-vessel basis for physiologic indices.

In keeping with major trials showing non-inferiority for iFR to FFR for clinical outcomes, treatment thresholds were a DPR of 0.89 and an FFR of 0.80 [2,3].

The primary hypothesis of this study was that, in keeping with recently published data, there is a higher discordance rate in the LAD compared to the non-LAD arteries. Post-hoc analysis of the DPR cut-off which offers the best diagnostic accuracy to predict FFR results in the most discordant artery was considered experimental and hypothesis generating.

2.1. Patient and lesion characteristics

110 patients underwent FFR and DPR of moderate coronary artery stenoses within the study period. 119 lesions were assessed for these 110 patients.

The average age was 62.8 years with age ranging from 37 to 84 years. 20.9% of patients were women. The mean ejection fraction (where known) was 55.3%.

Lesions were assessed in coronary arteries as outlined in Table 3. In brief, 59.6% of lesions were in the LAD (n = 71), 26.9% were in the RCA (n = 32) and 11.8% were in the LCx (n = 14). 1.7% of lesions were in the LMS (n = 2).

Lee et al. derived their data from the 3V FFR− FRIENDS study where all recruited patients underwent three-vessel physiologic assessment, therefore, by design their lesion distribution was in a roughly 1:1:1 ratio of LAD, right coronary artery and left circumflex artery lesions (293:276:306).

By contrast, the distribution of lesions in our study is more representative of a real-world sample. This is in keeping with the work of Hennigan et al. 2016, whose VERIFY 2 single-centre prospective study collected data from routine clinical care of consecutive patients undergoing FFR. The proportion of LAD, RCA and LCx lesions in our cohort (59.6%, 26.9% and 11.8% respectively) was comparable to that of the VERIFY 2 study (59.9%, 17.5% and 19.1% respectively), non-significantly different in separate two-sided z-tests for the equality of proportions (p = 0.518, p = 0.106 and p = 0.213 respectively) and cumulatively in a goodness- of-fit test (p = 0.106). Likewise, in comparison to the proportional distribution of lesions in the earlier RESOLVE study, our study sample did not have a significant difference.

Baseline demographics are outlined in Table 2.

2.2. Statistics

The statistical analysis was performed by a statistician (B.J.) who was independent of the clinical research team. All data analysis was performed using R (v. 3.6.3), an open-source programming language and software environment for statistical computing supported by the R Foundation for Statistical Computing [13].

Sample size calculations were performed using the "pwr" package in R [14]. To conduct the power calculation for our primary hypothesis, we assume a power of 0.8, a significance level of 0.05 and "Cohen's h" equal to 0.5 (i.e. a medium effect size for a comparison of two proportions) [14]. Since we are comparing between LAD and non-LAD lesions, we account for the expected asymmetry (i.e. the relative abundance of LAD lesions), since asymmetry of group size decreases the power of the comparison between two proportions. We do this by assuming 62% (154/248) of lesions to be LAD lesions, in accordance with results of the VERIFY 2 study [4]. This works out to a sample size of 105 (65.2 LAD and 39.8 non-LAD lesions). However, we then account for the assumed binomial variation of the proportion of each type of lesion in a sample, since we will sometimes have greater asymmetry than the

Table 2

Baseline characteristics for the 110 patients included in the study. Ejection fraction is reported for the 81 patients where this information was available. When compared to the patient characteristics outlined in the VERIFY 2 trial, our sample displayed no significant difference in rates of male sex, diabetes mellitus, hypertension and prior MI. Our sample did have a significantly higher proportion of patients with prior PCI (p = 0.0119).

Baseline Characteristics	n	(%)
Clinical Characteristics		
Male	87	(79)
Diabetes Mellitus	28	(25)
Hypertension	74	(67.3)
History of or current cigarette smoking	76	(69)
Previous MI	37	(33.6)
Previous PCI	47	(42.7)
Previous CABG	1	(0.9)
Vessels (n = 119)		
LAD	71	(59.7)
RCA	32	(26.9)
LCx	14	(11.8)
LMS	2	(1.7)
Arterial Dominance		
RCA	93	(78.1)
LCx	22	(18.5)
Co-dominant	4	(3.4)
Clinical Presentation		
Stable angina	8	(43.6)
Unstable angina	10	(9.1)
NSTEMI	23	(20.9)
Atypical chest pain	7	(6.4)
Convalescent STEMI	5	(4.5)
Heart failure	7	(6.4)
Arrhythmia	8	(7.3)
Pre-valve surgery/pre-operative angiography	2	(1.8)
Ejection Fraction (n = 81)		
Ejection Fraction >50%	55	(68)
Ejection Fraction 40–50%	22	(27)
Ejection Fraction <40%	4	(5)

Table 3

Characteristics of the 119 lesions assessed with DPR and FFR in this study on a per-vessel basis. Angulated lesions were those lesions with a ≥90-degree bend associated with the stenosis. Long lesions were those stenoses which measured ≥30 mm.

Lesion Characteristics	n	(%)
Left anterior descending (n = 71)		
Calcification		
Non-calcified	15	(21.1)
Mild	22	(31)
Moderate	26	(36.6)
Severe	8	(11.3)
Angulated	7	(9.9)
Eccentric	39	(55)
Side branch involvement	48	(67.6)
Long lesion	33	(46.5)
Arterial dominance		
RCA dominant circulation	51	(71.8)
LCx dominant circulation	17	(24)
Co-dominant circulation	3	(4.2)
Right coronary artery (n = 32)		
Calcification		
Non-calcified	10	(31.3)
Mild	10	(31.3)
Moderate	7	(21.9)
Severe	5	(15.6)
Angulated	18	(56.3)
Eccentric	23	(71.9)
Side branch involvement	17	(53.1)
Long lesion	16	(50)
Arterial dominance		
RCA dominant circulation	30	(93.8)
LCx dominant circulation	1	(3.1)
Co-dominant circulation	1	(3.1)
Left circumflex (n = 14)		
Calcification		
Non-calcified	5	(35.7)
Mild	3	(21.4)
Moderate	4	(28.6)
Severe	2	(14.3)
Angulated	2	(14.3)
Eccentric	10	(71.4)
Side branch involvement	6	(42.9)
Long lesion	6	(42.9)
Arterial dominance		
RCA dominant circulation	10	(71.4)
LCx dominant circulation	4	(28.6)
Co-dominant circulation	0	(0)

expected asymmetry by random variation (47.1% of the time). At 116.7 total lesions, we will randomly draw more than 35.6 non-LAD lesions, 90% of the time. While less than 39.8, this is sufficient in combination with the corresponding LAD lesions, as it yields a power of 0.8001. Hence, we take 117 total lesions as our sample size.

The main statistical test used was the two-proportion z-test for comparing two proportions of unequal size. The z-statistic is the difference of the two proportions divided by the standard error of the difference of the two proportions, calculated according to the default method from the "stats" package in R. A continuity correction, as described, for example, by Newcombe [15], is accepted according to the default method from the "stats" package. Pearson's χ^2-test was used for assessing independence and goodness of fit. Fisher's exact test was used where the expected value of >20% of the cells in the contingency table was less than 5.

The Clopper-Pearson method (the default in R) was used to compute 95% confidence intervals about a proportion. Where such an interval has been computed for an epidemiological measure (i.e., sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy), we have rounded to the nearest decimal point.

2.3. Analysis

In line with evidence-based practice, we considered clinically relevant ischaemia to be present when FFR was ≤0.80. Where a lesion extended from the proximal LAD into the mid-LAD it was considered within the category of the proximal LAD.

Accordingly, the performance of DPR compared to FFR in the three major epicardial coronary arteries was assessed using the following metrics:

Sensitivity – the proportion of positive FFR tests that are correctly identified by DPR
Specificity – the proportion of negative FFR tests that are correctly identified by DPR
Positive predictive value – the probability that a positive DPR predicted a positive FFR
Negative predictive value – the probability that a negative DPR predicted a negative FFR

3. Results

The mean FFR value was 0.858 with a minimum value of 0.69 and maximum value of 0.98. The mean dPR was 0.926 with minimum value of 0.78 and maximum of 1.01.

In keeping with previous studies, the overall sensitivity of DPR (using a cut off value of ≤0.89) was 90.9% (20/22) and the overall specificity was 91.8% (89/97).

The overall positive predictive value was 71.4% (20/28) and negative predictive value was 97.8% (89/91).

Table 4
A summary of the discordance rates between FFR and DPR on a per-vessel basis.

Discordant FFR and DPR	
All vessels	8.4% (10/119)
Left anterior descending	12.7% (9/71)
Right coronary artery	3.125% (1/32)
Left circumflex	0% (0/14)

The overall diagnostic accuracy of DPR to FFR in our group was 91.6% (109/119). By corollary, misclassification (discordance) between DPR and FFR occurred in 8.4% of lesions assessed (n = 10).

12.7% of LAD lesions assessed (n = 9/71) had discordant results. Non-LAD lesions (RCA and LCx) had a combined discordance rate of 2.4% (1/46). This represents a statistically significant increased rate of discordance in LAD lesions compared to non-LAD lesions (p = 0.04986).

The right coronary artery had a 3.125% discordance rate in this study (1/32). No LCx lesions had discordant results. However, analysis of discordance rates in the LCx was limited by the relatively low number of lesions assessed (Table 4).

There was no significant difference in the presence of discordant results between men and women.

3.1. Left anterior descending

We found that DPR had a sensitivity of 94.4% for detecting ischaemia in the LAD.

Specificity of DPR in the LAD was lower at 84.9% (of the 53 negative FFRs in the LAD, there were 45 true negative DPRs with 8 false positives).

The positive predictive value of DPR was 68% in the LAD (of the 25 positive DPR tests in the LAD, there were 17 positive FFRs). The eight false positive DPR results in the LAD were at, or close to the cut-off figure, either 0.88 or 0.89.

The negative predictive value of DPR was 97.8% with only one false negative DPR in the LAD see Table 5 and Fig. 1.

3.2. Right coronary artery

Sensitivity assessment for the RCA was limited in this study by the low number of patients with positive FFR in this artery. Only three out of 32 RCA lesions tested positive by FFR. DPR had a sensitivity of 66.7% for these three lesions in this study.

Specificity was 100% for a negative DPR, with 29 negative FFR tests corresponding to 29 negative DPRs.

Positive predictive value was 100% and negative predictive value was 96.6%.

3.3. Left circumflex and left main stem

14 lesions in the left circumflex artery were interrogated with FFR and DPR, 13 lesions were negative by FFR and DPR with 1 lesion positive. There was no DPR misclassifications in the left circumflex artery in this group of lesions.

Two left main stem lesions were negative by both FFR and DPR.

3.4. Proximal versus non-proximal left anterior descending

39.4% (n = 28) of LAD lesions assessed were in the proximal LAD, with the remaining 60.6% (n = 43) being mid- or distal-LAD lesions.

7.1% of lesions in the proximal LAD were discordant (2/28). Of the two discordant results, one was due to a false negative DPR with a positive FFR, the other was due to a false positive DPR with negative FFR.

16.3% of lesions in the mid- or distal-LAD were discordant (7/43). All cases of discordance in the mid- or distal-LAD were due to false positive DPR results of either 0.88 or 0.89 with negative FFR results.

Sensitivity of DPR in the proximal LAD was 85.7% with a specificity of 95.2%. Positive predictive value was 85.7% and negative predictive value was 95.2%.

Sensitivity of DPR in the non-proximal LAD was 100%, with specificity of 78.1%. Positive predictive value was 61.1% and negative predictive value was 100% (see Table 6 and Fig. 2).

3.5. Assessment of the sensitivity and positive predictive value of DPR for FFR in the non-proximal LAD with cut-off value of DPR adjusted to ≤0.87 or ≤0.88

In the patient's assessed in this study, note was made of a tendency for non-proximal LAD lesions to be associated with false positive DPR results in the borderline range, 0.88 and 0.89.

This resulted in a positive predictive value of 61.1% due to 7 false positives, all of which were either 0.88 or 0.89.

Likewise, the specificity was 78.1% for the same reason.

When the DPR cut-off was adjusted downwards (to ≤0.87) for lesions in the non-proximal LAD, the positive predictive value increased to 100%, the sensitivity fell to 81.8%, specificity increased to 100% and the NPV remained acceptable at 94.1%.

When the DPR cut-off was adjusted downwards to ≤0.88, lesions in the non-proximal LAD, the positive predictive value increased to 78.6%, the sensitivity remained at 100%, specificity increased to 90.6% and the negative predictive value remained at 100% (see Table 7).

4. Discussion

The Long-Term Clinical Outcomes of NHPRs Study (Lee et al. 2020 [10]) assessed the relationship between discordant FFR and non-hyperaemic pressure ratios and a 5-year vessel-oriented composite outcome (VOCO). Deferred discordant lesions had a cumulative incidence of VOCO of 14.4%. Meanwhile deferred concordant negative lesions had a cumulative incidence of VOCO of 7.5%. In the per-vessel breakdown 12.9% of LAD lesions were discordant compared to 5.43% of RCA lesions and 1.63% of LCx lesions. This disproportionate discordance rate led to the primary hypothesis of this study: namely, that there would be a higher discordance rate between FFR and DPR in the LAD compared to the non-LAD arteries [10].

This finding from Lee et al. of a higher rate of discordance between FFR and NHPR in the LAD is in contrast to the RESOLVE study, where no significant differences in diagnostic accuracy were noted when LAD coronary artery stenoses were compared with non-LAD coronary artery stenoses [2].

However, differences existed between these two studies, including iFR cut-offs of 0.89 and 0.90 respectively.

We identified a 12.7% discordance rate in the LAD. This was similar to the 12.9% discordance rate in LAD lesions assessed in the Long-Term Clinical Outcomes of NHPRs Study and represented a statistically significant increased rate of discordance in LAD lesions when compared to non-LAD lesions.

We found an overall discordance rate of 8.4% in all lesions assessed. This is lower than was found in the RESOLVE study (19.6%) and the VERIFY 2 trial (21%), although the iFR cut-off in these studies for positive iFR was 0.90 [2,4].

Other authors have described a reduced sensitivity of iFR for FFR in the right coronary versus the left coronary artery, but with an improved specificity [11,12]. We found a similar numeric in our group when comparing sensitivity and specificity in the LAD versus

Table 5

Sensitivity, specificity, positive predictive value and negative predictive value of DPR for FFR in the LAD and RCA, and in the proximal and non-proximal LAD.

Vessel	Sensitivity	Specificity	PPV	NPV
Left anterior descending **(Confidence interval)**	**94.4%** (17/18) (73–100%)	**84.9%** (45/53) (72–93%)	**68.0%** (17/25) (46–85%)	**97.8%** (45/46) (88–100%)
Right coronary artery **(Confidence interval)**	**66.7%** (2/3) (9–99%)	**100%** (29/29) (88–100%)	**100%** (2/2) (16–100%)	**96.6%** (29/30) (83–100%)

Table 6

Sensitivity, specificity, positive predictive value and negative predictive value of DPR for FFR in the LAD and RCA, and in the proximal and non-proximal LAD.

Vessel	Sensitivity	Specificity	PPV	NPV
Proximal LAD **(Confidence interval)**	**85.7%** (6/7) (42–100%)	**95.2%** (20/21) (76–100%)	**85.7%** (6/7) (42–100%)	**95.2%** (20/21) (76–100%)
Mid- or distal-LAD **(Confidence interval)**	**100%** (11/11) (72–100%)	**78.1%** (25/32) (60–91%)	**61.1%** (11/18) (36–83%)	**100%** (25/25) (86–100%)

Table 7

The sensitivity, specificity, positive predictive and negative predictive value, and overall diagnostic accuracy in the non-proximal LAD at differing DPR cut-off values.

DPR cut off in non-proximal LAD	≤0.89	≤0.88	≤0.87
Sensitivity	100%	100%	81.8%
Specificity	78.1%	90.6%	100%
Positive predictive value	61.1%	78.6%	100%
Negative predictive value	100%	100%	94.1%
Overall diagnostic accuracy	83.7%	93%	95.3%
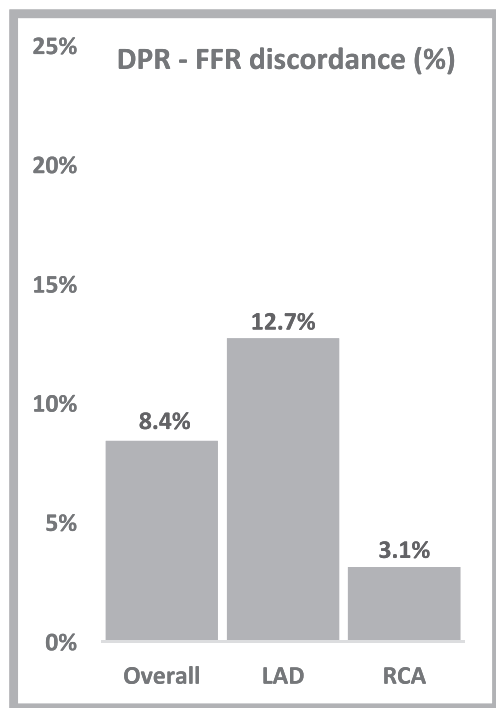
Fig. 1. DPR and FFR discordance/misclassification in the LAD compared to the RCA.

Fig. 2. DPR and FFR discordance/misclassification in the proximal LAD compared to the non-proximal LAD.

the right coronary artery. These findings have been attributed to different flow distribution between systole and diastole in the RCA compared to the left coronary artery.

Other studies have addressed outcomes for lesions with discordant FFR and NHPRs.
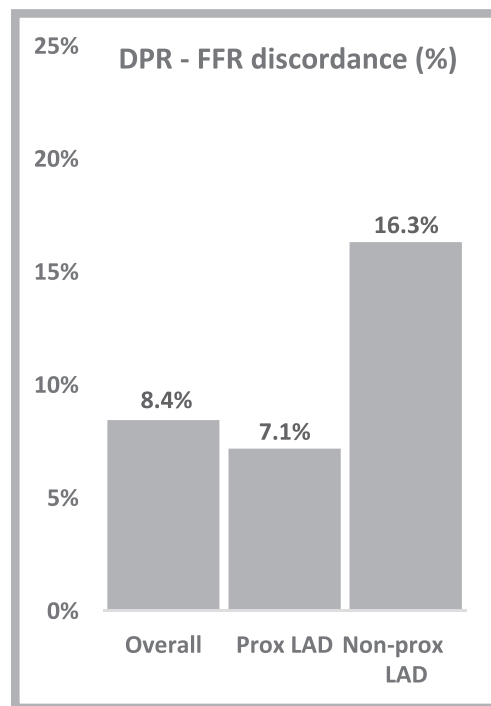
Lee et al. (2017) compared the rate of major adverse cardiac events (MACE) at 2 years in patients with concordant normal, concordant abnormal and discordant FFR and iFR. Patients with discordant results did not show a significant higher risk of MACE compared to patients with concordant normal FFR and iFR. The discordance rates between each coronary artery were not provided in the study. The presence of diabetes mellitus was a predictor of discordance in the FFR−/iFR+ group in this study [6].

Cook et al. (2017) compared coronary flow characteristics between FFR-iFR discordant lesions and angiographically unobstructed vessels. They found that hyperaemic flow velocity and coronary flow reserve were similar between patients with FFR+/iFR− lesions and concordant negative lesions as well as patients with unobstructed vessels. In FFR−/iFR+ discordants, hyperaemic
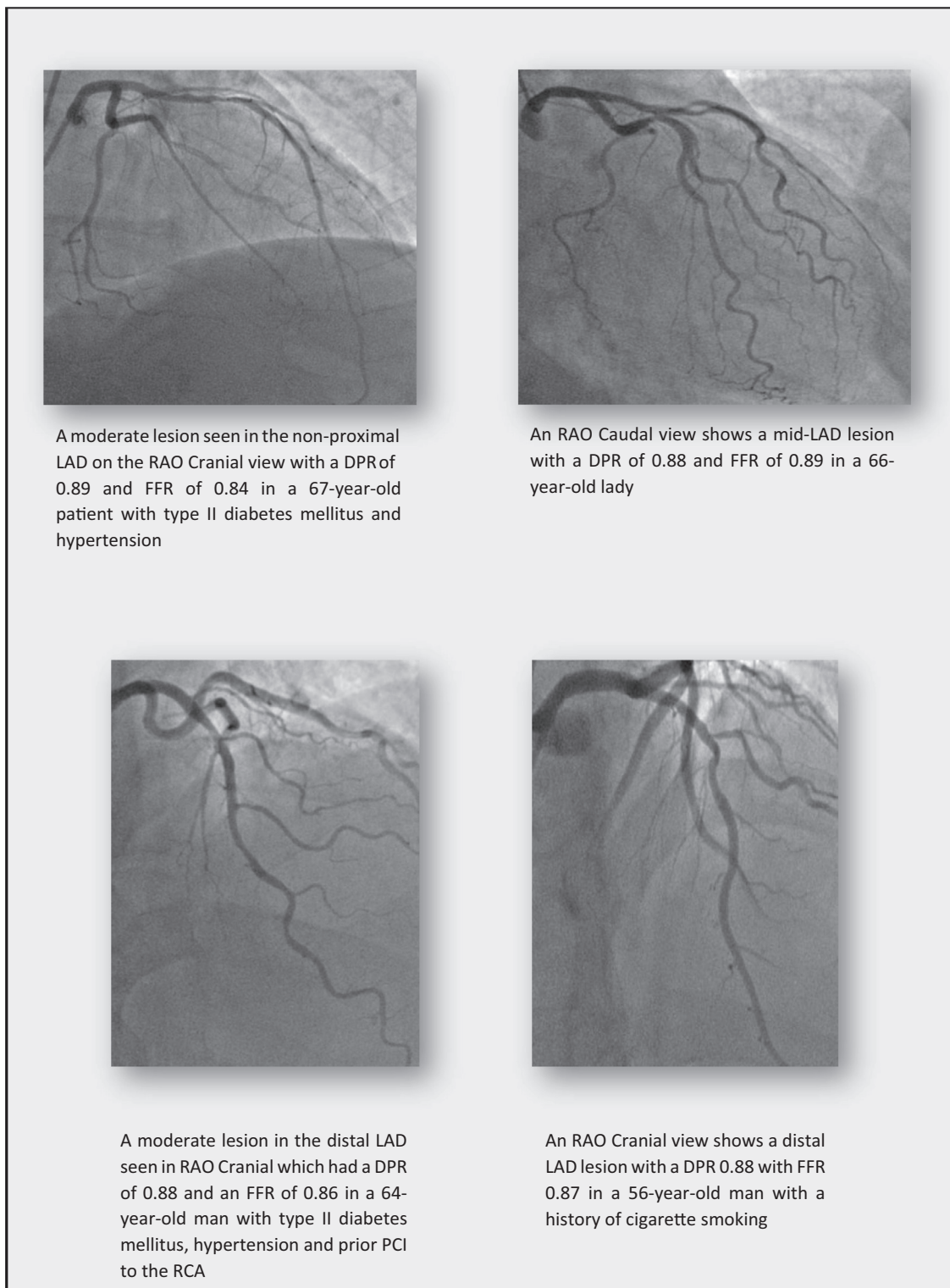
A moderate lesion seen in the non-proximal LAD on the RAO Cranial view with a DPR of 0.89 and FFR of 0.84 in a 67-year-old patient with type II diabetes mellitus and hypertension

An RAO Caudal view shows a mid-LAD lesion with a DPR of 0.88 and FFR of 0.89 in a 66-year-old lady

A moderate lesion in the distal LAD seen in RAO Cranial which had a DPR of 0.88 and an FFR of 0.86 in a 64-year-old man with type II diabetes mellitus, hypertension and prior PCI to the RCA

An RAO Cranial view shows a distal LAD lesion with a DPR 0.88 with FFR 0.87 in a 56-year-old man with a history of cigarette smoking

Fig. 3. Angiographic examples of non-proximal LAD lesions with false positive DPR.

flow velocity and coronary flow reserve were similar to the concordant positive group. There was a significantly higher rate of diabetes mellitus in the FFR−/iFR+ group (41.7%) compared to the FFR+/iFR− group (13.6%) (p = 0.03) [5].

Lee et al. (2019) carried out a prospective study to evaluate the physiologic characteristics and five-year patient oriented composite outcome of patients with discordance between FFR and iFR. In keeping with Cook et al. patients with FFR−/iFR+ lesions had similar CFR to patients with concordant positive lesions. In patients with FFR+/iFR- lesions, CFR was similar to the control group. Only patients with concordant positive FFR and iFR had a higher patient-oriented composite outcome compared with the concordant negative group. The discordance rates between coronary arteries were not provided. In this study, in agreement with Cook et al. (2017) and Lee et al. (2017), the FFR−/iFR+ group had a higher rate of diabetes mellitus. This group were also identified as having a

higher rate of patients with ACS versus the FFR+/iFR- group (27.8% vs 19%) [9].

Kobayashi et al. (2016) evaluated the effect of lesion location on the diagnostic accuracy of iFR, Pd/Pa and contrast FFR. They found these adenosine free indices to be less accurate in the left main/proximal LAD compared to other lesion locations. They hypothesised that this is likely related to the greater territory supplied by these locations and the change in coronary flow from rest to maximal hyperaemia is greater in vessels supplying greater amounts of myocardium. Contrast FFR provided the best diagnostic accuracy among the adenosine-free indices, regardless of lesion location [16].

The current study is a real-world dataset of consecutive patients attending for coronary angiography at our centre. While this is a single-centre study, it nonetheless provides supplementary data to the field and is comparable in many regards to other published data on the topic.

Many studies on the topic of discordant coronary artery lesions describe clinical outcome data and outline clinical characteristics of discordant lesions. This was beyond the scope of the current analysis, which rather sought to test the hypothesis that the left anterior descending artery was the greatest producer of discordant lesions.

It would have been advantageous to perform an analysis with adequate power to detect confounders which might otherwise explain the variation in discordance rates. Nevertheless, the sample in this study would not suffice for such an analysis and would require a purpose-built recruitment protocol or a cohort derived from a big-data source.

The finding of a higher discordance rate in the LAD compared to the non-LAD coronary arteries is in keeping with data from Lee et al. (2020) and Kobayashi et al. (2016). The smaller sample size in our study was nevertheless a limitation that these studies did not encounter.

In addition to our primary hypothesis, in a post hoc analysis we explored discordance rates in the proximal and non-proximal segments of the LAD. This was driven by an interest in identifying if one segment of the artery had a disproportionate contribution to the overall discordance rate. Through this analysis, the phenomenon of DPR positive and FFR negative lesions were noted most in non-proximal LAD lesions.

As a hypothetical measure, we found that in our group of patients with non-proximal LAD lesions, adjusting the DPR cutoff to 0.87 increased the positive predictive value, and improved the overall diagnostic accuracy of the test from 83.7% to 95.3%. This was for speculative purposes and the numbers included were too small to draw a real-world conclusion from this post-hoc analysis. Nevertheless, it is fathomable that improvements in the diagnostic accuracy of DPR for FFR may be improved by tailoring DPR cut-offs to the location of the lesion assessed.

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Declaration of Competing Interest

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