Journal of Advances in Medicine and Medical Research

34(23): 202-209, 2022; Article no.JAMMR.93223
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Routine Use of Pressure Wire as an Adjunct to Diagnostic Angiography; Comparison of Resources Utilization in the Catheterization Laboratory: A Sub-Study of RIPCORD 2

Yousra Aboul-Enien [a*], Nick Curzen [b], Magdy Elmasry [a], Hanan Kassem [a], Ehab Hamdy [a], Mahmoud El-Amrousy [a], Liam Mullen [c], Mostafa Elguindy [c], Ian Kemp [c], Zoe Nicholas [b] and Rod Stables [c]

[a] Tanta University Hospital, Tanta, Egypt.
[b] Southampton University Hospital, UK.
[c] Liverpool Heart and Chest Hospital, UK.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2022/v34i234855

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/93223

Original Research Article

Received 02 September 2022
Accepted 03 November 2022
Published 08 November 2022

ABSTRACT

Background: The RIPCORD 2 trial randomized patients undergoing coronary angiography to strategy of routine measurement of fractional flow reserve (FFR) in all vessels or to angiography alone.
Objectives: We compared, for the randomized groups, the catheter laboratory procedure costs to diagnosis.
Methods: This is a sub-study of the RIPCORD2 trial. We excluded patients with follow-on PCI to better reflect procedural costs of the diagnostic phase. We compared resource utilization and, from this, derived an estimated procedure cost for UK practice. We examined the association between cost and the number of vessels examined with pressure wire (PW) technology.
Results: We included 249/552 (45%) patients randomized to angiography and 261/548 (48%) patients to systematic FFR measurement. The median (IQR) procedure cost was higher in the FFR group £1392 (1126 – 1686) versus £411 (308 – 586); P < 0.001. In the FFR group, 86.6% of

**Corresponding author;*

procedures were completed with a single pressure wire; two and three PWs were used in 10.7% and 1.5% of cases respectively. The procedure duration (median, IQR; mins) was longer in the FFR group; 52 (39 – 66) versus 20 (15 – 30) as was the use of radiographic contrast (median, IQR; mls); 140 (110 – 189) versus 70 (60 – 94). In the FFR group, it seems that the additional cost was associated with the cost of the PW and laboratory set up for the performance of FFR measurement; the incremental cost of examining additional vessels, beyond the first, was modest.
Conclusion: The procedural cost associated with a strategy of systematic measurement of FFR in all vessels is higher than that of angiography alone.

Keywords: Catheterization laboratory; diagnostic angiography; pressure wire; RIPCORD 2.

1. INTRODUCTION

Ischemic heart disease (IHD) is one of the leading causes of death and premature mortality worldwide [1]. The World Heart Federation expects that the global cost of CVD that arise from hospitalizations, treatments, revascularization procedures, clinic visits, emergency visits, and prescribed drug treatments to rise to more than US$1 trillion by 2030 [2]. This huge clinical and economic burden of IHD mandates seeking cost effective diagnostic and management strategies.

Myocardial ischemia is considered one of the most important risk factors for adverse outcomes in coronary artery disease (CAD) patients, therefore its detection is crucial for revascularization decisions [3,4]. Although invasive coronary angiography has been the gold standard for diagnosing coronary artery disease for several decades, the association between angiographic appearance and resulting ischemia is less clear than generally assumed [5]. In addition to non-invasive stress tests, ischemia can be also assessed accurately, and at low rate of complications during coronary angiography by means of intracoronary pressure wire assessment, typically measuring fractional flow reserve (FFR) [6].

Several trials have been conducted on the short and long term clinical and economic outcomes of using FFR in guiding revascularization strategy [7,8,9,10,11,12]. However, the impact of routine systematic use of pressure wire at the stage of diagnostic angiography on resources utilization in catheterization laboratory (cath lab) has not been widely studied. This issue was examined in the recently published RIPCORD 2 trial [13,14]. This sub-analysis of RIPCORD 2 will focus on comparing resource utilization in cath lab between patients who had invasive angiography only versus invasive angiography with routine performance of FFR.

2. METHODS

2.1 Study Design

We used data from the RIPCORD 2 study which was an open-label, prospective; multi-center randomized controlled trial that compared two strategies for the investigation of coronary artery disease at the time of angiography.

2.2 Study Population

The design and principal results of RIPCORD 2 have been published [13,14]. In brief, the study included 1100 patients recruited from 17 UK centers who presented with stable angina or stabilized acute coronary syndrome (ACS) in the period between September 2016 and June 2018. These patients were randomized to conventional angiography or additional routine pressure wire assessment to measure fractional flow reserve (FFR) in all main vessels judged as being of sufficient vessel caliber to allow percutaneous coronary intervention (PCI). Some patients in both groups were managed with 'follow-on' PCI during the same procedure. For this analysis, these patients (n = 590) have been excluded. We included 249/552 (45%) patients randomized to angiography and 261/548 (48%) patients to systematic FFR measurement to allow direct and specific comparison of resource utilization associated with the two investigation strategies (Fig. 1).

2.3 Study Outcome Measures

The primary outcome measure of this sub-analysis was a comparison of the two diagnostic strategies in terms of the total procedure cost. This was calculated from the costs of equipment utilization, procedure time and contrast volume. Subgroup analysis was performed for the number of vessels examined by PW technology and its impact on the procedure cost.

2.4 Cost Calculation

The procedure cost was calculated from the costs of the materials used during the procedure (diagnostic catheters, guiding catheters, pressure wires, OCT, IVUS, Adenosine, radiographic contrast) and the cost associated with the procedure duration. A procedural cost was determined for each patient, and we present descriptive and comparative statistics for the randomized groups. These cost references were obtained from routine costs incurred at the Liverpool Heart and Chest Hospital, but these values would be typical for most UK hospitals (Table 1).

2.5 Statistical Analysis

The normality of continuous variables was evaluated by a visual inspection of histograms, and by Shapiro-Wilk tests. All the variables of this sub-study had a non-normal distribution and are reported as medians and inter-quartile range (IQR). Categorical variables are expressed as counts and percentages. Statistical analyses were performed using SPSS statistical package, Version 24 (IBM Corp., Armonk, NY, USA). We performed comparative tests using Mann Whitney U test for medians. P-values are two-sided, and a p-value <0.05 was considered statistically significant.

Table 1. Unit costs for items included in the cost model

Resources	Unit Cost
Diagnostic catheter	£6.50
Guide catheter	£20.00
Pressure wire	£315.00
OCT	£600.00
IVUS	£475.00
Adenosine cost per patient	£12.00
Contrast per ml	£0.05
Cost per minute of lab time	£19.00

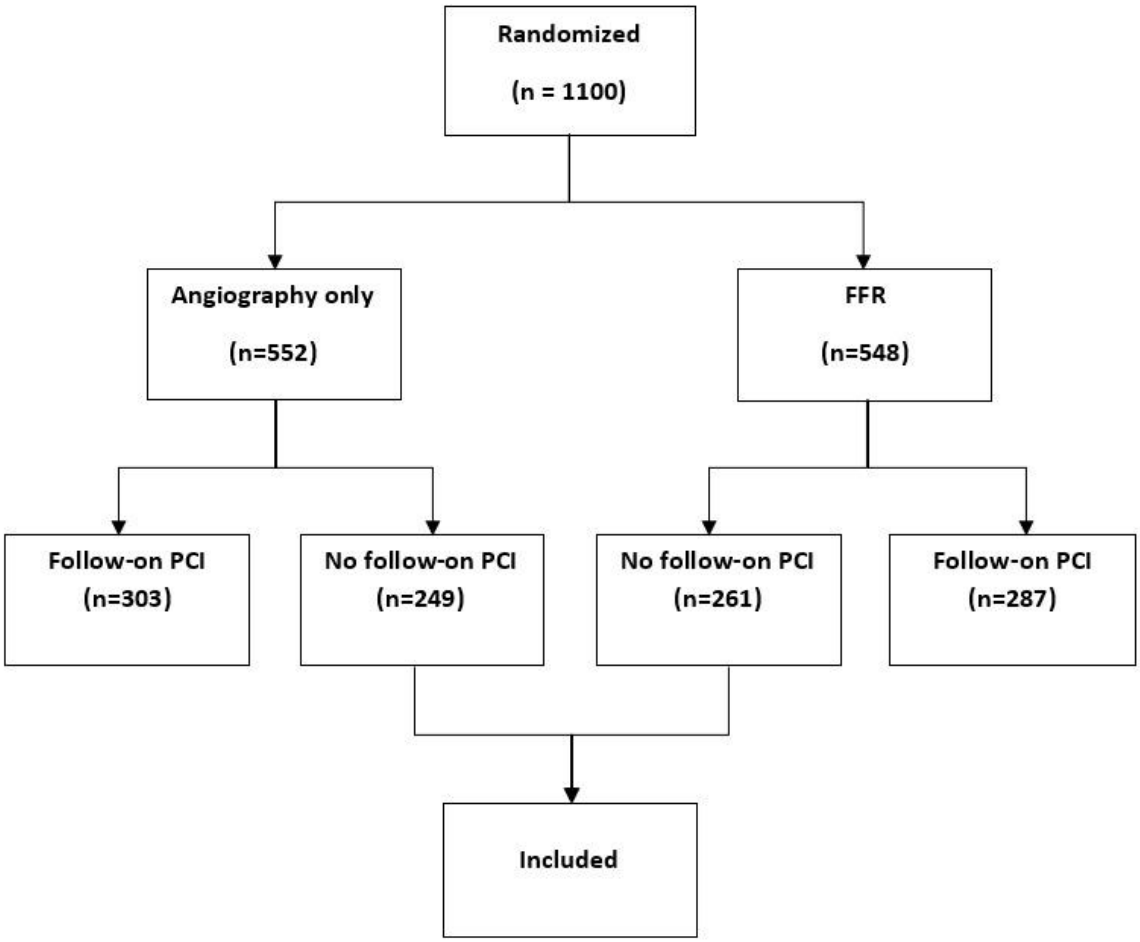

Fig. 1. Patient flow chart

3. RESULTS

We included in our sub-analysis 249/552 (45%) patients randomized to angiography only and 261/548 (48%) patients randomized to systematic FFR measurement (Fig. 1).

The median (IQR) of the total procedure costs in £ was significantly higher in the FFR group £1392.00 (1126 -1686) versus £411.50 (308 - 586) in the angiography only group; P <0.001 (Table 2). We also compared the equipment utilization, contrast dose in ml and the procedure duration in minutes in both groups as they are the cost drivers. The descriptive statistics for the frequencies and percentages of diagnostic catheters, guiding catheters, pressure wires, and IVUS and OCT catheters used is shown in (Table 2). In terms of the procedure time, there was significant difference between the two groups where the FFR group showed higher median (IQR) of procedure time; 52 (39 - 65.7) minutes versus 20 (15 - 30) minutes in the angiography group; P < 0.001 (Table 3). Additionally, on comparing the contrast dose in ml, the FFR group showed significantly higher median (IQR) contrast dose 140 (110 - 188.75) ml versus 70 (60 - 94) ml in the angiography group; P <0.001 (Table 2).

In a Post-Hoc analysis, based on treatment received, rather than intention to treat, we analyzed the number of vessels that were examined with pressure wire in our study population. We found that 253(49.6%) patients did not have any vessels examined with pressure wires.

Table 2. Descriptive and comparative statistics for total procedure cost, procedure time and resource utilization

	Angiography (n=249)	FFR (n=261)	Significance
Number of diagnostic catheters, n (p%)			
0	12 (4.8%)	12 (4.6%)	
1	55 (22.1%)	64 (24.5%)	
2	131 (52.6%)	154 (59%)	
3	47 (18.9%)	26 (10.0%)	
4	3 (1.2%)	3 (1.1%)	
5	0 (0.0%)	1 (0.1%)	
6	1 (0.4%)	1 (0.4%)	
Number of Guiding catheters, n (p%)			
0	173 (69.5%)	2 (0.8%)	
1	63 (25.3%)	71 (27.2%)	
2	11 (4.4%)	169 (64.8%)	
3	1 (0.4%)	16 (6.1%)	
4	1 (0.4%)	0 (0.0%)	
5	0 (0.0%)	2 (0.8%)	
6	0 (0.0%)	0 (0.0%)	
7	0 (0.0%)	1 (0.4%)	
Number of pressure wires, n (p%)			
0	248 (99.6%)	3 (1.1%)	
1	1 (0.4%)	226 (86.6%)	
2	0 (0.0%)	28 (10.7%)	
3	0 (0.0%)	4 (1.5%)	
Number of IVUS catheters, n (p%)			
0	247 (99.2%)	261 (100%)	
1	2 (0.8%)	0 (0.0%)	
Number of OCT catheters, n (p%)			
0	249 (100%)	260 (96.6%)	
1	0 (0.0%)	1 (0.4%)	
Procedure time minutes, median (IQR)	20 (15 - 30)	52 (39 - 65)	P <0.001*
Contrast dose ml, median (IQR)	70 (60 - 94)	140 (110 - 188)	P <0.001*
Procedure cost £, median (IQR)	411 (308 - 586)	1392(1126 - 1686)	P <0.001*

Most of these patients belonged to the angiography group while 4 of them represented a cross-over from the FFR group. On the other hand, 257 (50.4%) patients had FFR assessment to at least one of their coronary arteries. One of these patients represented a cross-over from the angiography only group. Table 3 shows the number and proportion of patients with PW examination of 0, 1 or more vessels.

As a secondary outcome, we studied the impact of number of vessels examined with pressure wire on the procedure cost in UK £ and we found that the additional cost of FFR use was mainly related to the cost of the wire and initial setup; while the incremental cost associated with the examination of multiple vessels in a case was modest (Fig. 2).

4. DISCUSSION AND CONCLUSION

Despite the proven benefit of using FFR in guiding coronary artery revascularization, established in many trials [7,8,9,10,11,12], its use is more limited than we might expect. In the UK, the rate of PW use at the time of angiography has been reported at about 5% annually. The comparable figure for PW use in conjunction with PCI is 10 % [15]. In addition to the requirement of a skilled operator, the small risk of complication, and the cost of the procedure are also contributing factors to less wide-spread use of pressure wire approaches.

The RIPCORD 2 trial is the first completed randomized clinical trial that studied the economic and clinical outcomes of performing routine FFR in all sizable epicardial vessels at the time of diagnostic angiography in patients with stable angina or stabilized non–ST-segment–elevation acute coronary syndromes. The study proved that, over a one year follow up period, routine systematic FFR use was cost neutral compared with angiographic guidance alone and was not associated with significant differences in quality of life or angina status after 1 year of follow up. These costs were calculated based on the NHS Tariff system and included the costs starting from the index procedure and all subsequent hospital admissions, outpatient visits, and accident and emergency department attendance over the following year [14].

Table 3. Descriptive statistics of number of vessels examined with pressure wire

Number of vessels examined with pressure wire	0*	1#	2	3	4	5	6	7
Number of patients (%)	254 (49.6%)	9 (1.8%)	9 (1.8%)	61 (12%)	91 (17.8%)	62 (12.2%)	21 (4.1%)	4 (0.8%)

** Group 0 includes n=3 cross-over patients initially randomized to FFR group.*
 # Group 1 includes n=1 cross-over patient initially randomized to angiography group.

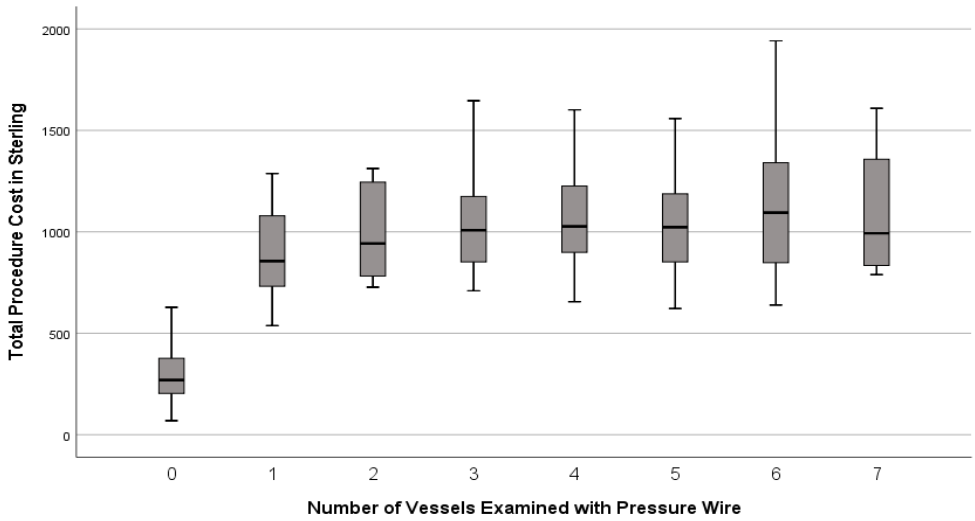

Fig. 2. Impact of number of vessels examined with pressure wire on the procedure cost in £

The aim of this sub-study was to perform a more detailed analysis of the procedural costs, based on a consideration of resource consumption, at patient level.

Unlike the main study, we calculated the procedure cost from the prices of the materials used during the procedure (diagnostic catheters, guiding catheters, pressure wires, OCT, IVUS, adenosine, radiographic contrast) and the cost associated with the procedure duration. These cost references were obtained from routine costs incurred at the Liverpool Heart and Chest Hospital catheterization lab which would be typical for most UK hospitals. The advantage of this method of costing that it will be more applicable and easily allowing comparison between studies held in countries that may have different unit costs.

The main finding of this sub-analysis was that performing routine FFR during diagnostic angiography led to a significantly higher median (IQR) procedure cost in the FFR group £1392 (1126 – 1686) versus £411 (308 – 586) in the angiography only group; $P < 0.001$. This resulted mainly from the additional cost of the PW which was (315 £) in our cost model. In the FFR group, 86.6% of procedures were completed with a single PW; two and three PWs were used in 10.7% and 1.5% of cases respectively. The procedure duration (median, IQR; mins) was longer in the FFR group; 52 (39 – 66) versus 20 (15 – 30) as was the use of radiographic contrast (median, IQR; mls) 140 (110 – 189) versus 70 (60 – 94).

The cost model of this sub-study was different from that used in one of FAMOUS NSTEMI sub-studies which aimed to evaluate the cost effectiveness of FFR compared with standard coronary angiography in 350 patients with NSTEMI. They included resources used for one-year: procedure related materials, hospitalizations, medical & health professional service use and clinical events, while in our study we focused on the index procedure costs. They found that more targeted invasive management can reduce healthcare resource costs without compromising patient outcomes which drove them to conclude that FFR-guided management of NSTEMI may be a cost-effective strategy over standard angiography. Unlike the results of the RIPCORD 2 trial [14], the cost savings they found were due to absolute, but non-significant, reductions in length of stay and health events such as revascularizations, re-hospitalizations, myocardial infarction and stroke events. However, due to the small sample size and the need for longer follow up, there still remains considerable decision uncertainty [16].

We studied the impact of the number of the vessels examined by the pressure wire on the procedure cost. The results showed that there was an obvious step-up in the cost when a pressure wire was used to examine the first vessel, however the incremental cost associated with examining additional vessels was modest. This finding may encourage operators to consider more widespread examination of the coronary vasculature once they had decided that flow physiology was required in at least one vessel.

The use of pressure wires will still have its strengths which were mentioned in the literature as easiness of use by expert interventionist, reliable results, prompt decision making, and lack of affectability by hemodynamics and patient characteristics. Additionally, its use will continue to be beneficial in selected cases of stable angina who do not have conclusive results or those who are not suitable for noninvasive tests, in patients with multiple vessel or diffuse coronary artery disease to guide the revascularization decisions. FFR will still be also useful to assess bifurcations and avoid unnecessary branch vessel stenting [17,18,19,20]. Moreover, their use in stabilized NSTEMI cases for the assessment of non-culprit vessels was found to direct more patients towards medical treatment rather than revascularization [12].

Our sub-study had some limitations. Our examination was restricted to diagnostic procedures; the incremental cost of PW use in cases that involved follow-on PCI may be less significant, as a proportion of total cost. Beyond this, the potential for cost differential related to more or less intervention in cases involving FFR was not examined. We did not record the amount of adenosine used for each patient in the FFR group and used a typical unit cost per patient in our calculations. Our comparison was limited to the cath-lab diagnostic procedure phase only, and we ignored the potential for cost differential in non-invasive and other testing before and after the index procedure.

CONSENT AND ETHICAL APPROVAL

The RIPCORD 2 trial was conducted according to the principles of the International Conference

on Harmonization–Good Clinical Practice standards, the Declaration of Helsinki, and National Health Service (NHS) Research Governance guidelines. The study protocol, patient information sheet, and consent form were approved by the National Research Ethics Service before the trial was started (Research Ethics Committee reference 16/LO/0570). All patients gave informed consent for participation. The study was registered before inclusion of the first patient at ClinicalTrials.gov (NCT02892903).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SK, AlKatheeri R, Alblooshi FM, Almatrooshi ME, Alzaabi ME, Al Darmaki RS, Lootah SN. Global Epidemiology of Ischemic Heart Disease: Results from the global burden of disease study. Cureus. 2020;12(7).
2. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P. The economic burden of cardiovascular disease and hypertension in low-and middle-income countries: A systematic review. BMC Public Health. 2018;18(1): 975.
3. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, Vant Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG, Ver Lee PN. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. New England Journal of Medicine. 2009;360(3):213-24.
4. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Jüni P. 2018 ESC/EACTS guidelines on myocardial revascularization. European Heart Journal. 2019;40(2):87-165.
5. Kern MJ, Samady H. Current concepts of integrated coronary physiology in the catheterization laboratory. Journal of the American College of Cardiology. 2010; 55(3):173-85.
6. Whittaker A, Curzen N. What has the RIPCORD trial told us about using fractional flow reserve for diagnostic angiography? Interventional Cardiology. 2013;5(6):593.
7. Pijls NH, van Schaardenburgh P, Manoharan G, Boersma E, Bech JW, van't Veer M, Bär F, Hoorntje J, Koolen J, Wijns W, de Bruyne B. Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study. Journal of the American College of Cardiology. 2007;49(21):2105-11.
8. Zimmermann FM, Ferrara A, Johnson NP, Van Nunen LX, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR. Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial. European Heart Journal. 2015;36(45): 3182-8.
9. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, van't Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. Journal of the American College of Cardiology. 2010;56(3):177-84.
10. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, Witt N, Kala P. Fractional flow reserve–guided PCI versus medical therapy in stable coronary disease. New England Journal of Medicine. 2012;367(11):991-1001.
11. Fearon WF, Bornschein B, Tonino PA, Gothe RM, Bruyne BD, Pijls NH, Siebert U. Economic evaluation of fractional flow reserve–guided percutaneous coronary intervention in patients with multivessel disease. Circulation. 2010;122(24):2545-50.
12. Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, Junejo S, Ahmed N, Lee MM, Shaukat A, O'Donnell A. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: The British Heart Foundation FAMOUS–NSTEMI randomized trial. European Heart Journal. 2015;36(2):100-11.
13. Elguindy M, Stables R, Nicholas Z, Kemp I, Curzen N. Design and rationale of the RIPCORD 2 Trial (Does Routine Pressure Wire Assessment Influence Management

Strategy at Coronary Angiography for Diagnosis of Chest Pain?) A Randomized Controlled Trial to Compare Routine Pressure Wire Assessment with Conventional Angiography in the Management of Patients with Coronary Artery Disease. Circulation: Cardiovascular Quality and Outcomes. 2018;11(2): e004191.

14. Stables R, Mullen L, Elguindy M, Nicholas Z, Aboul-Enien Y, Kemp I, O'Kane P, Hobson A, Johnson T, Khan S, Wheatcroft S. Routine pressure wire assessment versus conventional angiography in the management of patients with coronary artery disease: The RIPCORD 2 trial. Circulation; 2022.
15. Ghobrial M, Haley HA, Gosling R, Rammohan V, Lawford PV, Hose DR, Gunn JP, Morris PD. The new role of diagnostic angiography in coronary physiological assessment. Heart. 2021; 107(10):783-9.
16. Nam J, Briggs A, Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, Junejo S, Eteiba H, Petrie MC. Fractional Flow Reserve (FFR) versus angiography in guiding management to optimise outcomes in non-ST segment elevation myocardial infarction (FAMOUS-NSTEMI) developmental trial: Cost-effectiveness using a mixed trial-and model-based methods. Cost Effectiveness and Resource Allocation. 2015;13(1): 1-9.
17. Corcoran D, Hennigan B, Berry C. Fractional flow reserve: A clinical perspective. The International Journal of Cardiovascular Imaging. 2017;33(7):961-74.
18. Jeremias A, Kirtane AJ, Stone GW. A test in context: Fractional flow reserve: Accuracy, prognostic implications, and limitations. Journal of the American College of Cardiology. 2017;69(22):2748-58.
19. Ahn JM, Zimmermann FM, Johnson NP, Shin ES, Koo BK, Lee PH, Park DW, Kang SJ, Lee SW, Kim YH, Lee CW. Fractional flow reserve and pressure-bounded coronary flow reserve to predict outcomes in coronary artery disease. European Heart Journal. 2017;38(25):1980-9.
20. Kogame N, Ono M, Kawashima H, Tomaniak M, Hara H, Leipsic J, Andreini D, Collet C, Patel MR, Tu S, Xu B. The impact of coronary physiology on contemporary clinical decision making. Cardiovascular Interventions. 2020;13(14): 1617-38.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/93223