Journal of Research in Medical and Dental Sciences
2018, Volume 6, Issue 2, Page No: 29-34

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Can we Use Contrast-FFR Instead of Adenosine-FFR for Evaluation of Intermediate Coronary Artery Stenosis?

Saeed Alipour Parsa,Gholamreza Amini*,Mohammad Hasan Namazi, Morteza Safi, Hossein Vakili, Habibollah Saadat

Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

DOI: 10.5455/jrmds.2018626

ABSTRACT

Coronary fractional flow reserve (FFR) has been advocated as the gold standard approach in assessment of the intermediate coronary stenosis. The aim of the current study was to delineate efficacy of contrast versus adenosine FFR. Recent literatures about the definition, features, clinical relevance, advantages/disadvantages of both aforementioned methods, were reviewed, scrutinized and reviewed. We searched through various databases such as National Library of Medicine (NLM), MEDLINE and PubMed up to August 2017. It appears credible that according to our brief review, clinical relevance of contrast-FFR is justified and due to its applicability, accessibility and budget friendly nature, it could be used as an alternative method of FFR measurement.

Key words: Adenosine Fractional Flow Reserve, Contrast Fractional Flow Reserve, Clinical Application, Features, Fractional Flow Reserve, Limitation

HOW TO CITE THIS ARTICLE: Saeed Alipour Parsa, Gholamreza Amini, Mohammad Hasan Namazi, Morteza Safi, Hossein Vakili, Habibollah Saadat, Can we Use Contrast-FFR Instead of Adenosine-FFR For Evaluation of Intermediate Coronary Artery Stenosis?, J Res Med Dent Sci, 2018, 6 (2): 29-34, DOI: 10.5455/jrmds.2018626

Corresponding author: Gholamreza Amini
e-mail✉: rezaamini77@gmail.com
Received: 28/11/2017
Accepted: 15/02/2018

INTRODUCTION

Coronary artery disease (CAD) is a foremost cause of morbidity in developed countries (1). Though the morbidity rate of this condition has been progressively alleviated during the past decades, it is still accountable for roughly one-third of all deaths in people older than 35 years (2-4).

The clinical importance of moderate coronary-artery-stenosis is hard to define. Fractional flow reserve (FFR) is considered as an invasive diagnostic guide to measure the physiological significance of these intermediate epicardial coronary artery stenoses. FFR is considered as the gold standard method in evaluation of the intermediate coronary artery stenoses (5). An FFR of 1.0 is widely accepted as normal. An FFR lower than 0.75-0.80 is generally considered to be associated with myocardial ischemia (6). Concept of using FFR as a physiologic indicator is based on two main reasons. First, due to nonquantitative nature of angiogram, it does not provide impeccable clinical guidance for decision making of these intermediate lesions, whereas FFR relies on physiologic rather than anatomic evidences. Next, making decision to do PCI or CABG relies on documentation of ischemia, which cannot be surely confirmed via angiography (22, 23, 24). Angiography lacks vital information regarding assessment of vascular lumen. Assessment of angiographic images is unreliable and daunting, since it is a two-dimensional image from a three-dimensional object, in addition it couldn't delineate lucid image regarding vascular characteristics, namely plaque size, length or peculiarity. Moreover, estimation of severity of coronary lesions by angiography poses other limitations in branch overlap, vessel foreshortening, calcified lesions, ostial lesions and contrast streaming that makes it inaccurate (30).

In 1990 novel concept of myocardial FFR was postulated by N. Pijls and B. De Bruyne. Indeed, application of this novel method for first time was tested and confirmed among animal samples and then it was tested in humans (7, 8). Various clinicians and scholars tend to reach a consensus regarding impeccable, harmless cutoff values for FFR. For instance, Pijls and colleagues (1996) postulated that FFR cutoff value of 0.75 maintains a positive predictive value of 100% and a negative predictive value of 88% to assess the manifestation of ischemia (9). In another study Pijls and colleagues (2015), postulated that deferral of PCI with respect to FFR was outstanding and morbidity rate or acute MI were less than 1% per year that couldn't be lowered more by stenting (10). Afterward, FFR concept was tested and validated in more convoluted circumstances such as multiple lesions, multivessel disease, in-stent restenosis, post-stenting, left main disease, bifurcation lesions (11-16). Regarding measuring FFR, it is critical to maintain highest vasodilation of two vascular regions, explicitly the epicardial and microvascular arteries. If optimum vasodilation is not achieved, the FFR will be overestimated due to lower measurement of pressure gradient across the lesion. Various hyperemic stimulants have been proposed so far, i.e. adenosine, adenosine 5'-triphosphate (ATP), and papaverine (18-21). Aforementioned stimulants are administered through IV infusion or intracoronary (IC) bolus injection (17).

FFR practicalities:

- Catheters
- Wires
- Hyperemia
- Anticoagulation (17)

FFR procedure:

- Anticoagulation, i.e. IV heparin or bivalirudin
- IC nitroglycerin
- Connecting pressure wire to pressure analyzer device and modify the wire according to the atmospheric pressure out of body
- Wiring up tip of the catheter and making sure to be fully covered
- The wire is advanced through the guide to the coronary artery and guiding pressure are equalized before crossing the lesion at the tip of the guide
- Moving catheter throughout the stenosis (2 cm distal to the coronary lesion)
- Inducing hyperemia via IV adenosine (140 mcg/kg/min), IC bolus adenosine (20-30 mcg regarding right coronary artery, 60 mcg or 100 mcg with respect to left coronary artery).
- Obtaining FFR, which is calculated via Pd/Pa at the base of distal pressure acknowledged to be the point of maximal hyperemia
- PCI's pressure wire can be simultaneously used as angioplasty guide wire as well
- Ultimately, the wire is pulled back into guide (25).

* Dosage/Speed in administration of Contrast:

After baseline Pd/Pa was calculated, a single contrast medium injection of 6 ml (3 ml/s) was performed manually. Within 10 s after the contrast medium injection, the contrast medium induced Pd/Pa ratio was gauged (29, 36).

DISCUSSION

Abovementioned FFR procedure is more less the same with respect to various hyperemia stimulants. Pragmatically speaking, ideal hyperemia agent should maintain following characteristics, namely, low cost, minimal side effect, fast start and short duration (17).

IV adenosine tends to be the widely acceptable approach regarding inducing hyperemia due to its stable state and maintaining continual hyperemia. Adenosine's action onset is fast, it maintains short fast half-life less than 10 seconds. This half-life would enable the clinician to easily and slowly pullback the pressure wire. This feature is useful, when clinicians want to spot specific location of drop-off for both single/multi lesions. Assessment of aorto-ostial narrowing via IV adenosine is feasible, without experiencing catheter impediment due to maintaining maximal coronary flow (18). With respect to comparing efficacy of IV adenosine over adenosine IC procedure, Jeremias and Colleagues (2000), postulated that elevated doses of IC adenosine (>60 mcg) might improve hyperemia and generate lower FFR values (24, 25). In current review we aim to tackle subject regarding Efficacy of Adenosine FFR versus Contrast FFR, we are going to delineate hyperemia practicality a bit more.

Injection of contrast media and hyperemia stimulants: FFRcont, which is regularly used to assess the FFR guidewire location, likewise induces

hyperemia and may be an alternate method of measuring the FFR. In a study conducted by Nobuo and Colleagues (2017), they assessed Contrast-induced Hyperemia as Substitute to Drug-induced Hyperemia in the assessment of the Fractional Flow Reserve in Coronary Lesions. They announced that since inducing hyperemia via adenosine may cause rhythmic complications. The postulated that with threshold value of 0.82 and excellent sensitivity and a negative predictive value, FFRcont is considered as alternative approach of inducing hyperemia. Consistent with the subject of current study, Selim and Colleagues(2016), compared Efficacy of coronary fractional flow reserve using contrast medium compared to adenosine. They proposed that FFR measurements via contrast is practicable and characterize a novel index in the measurement of hemodynamically substantial coronary stenoses as a substitution to adenosine. Due to potential side effects of adenosine such as infusion, timewasting and even higher price in comparing to contrast, which is more accessible and cheaper comparing to adenosine. Furthermore, in Selim's study it is reported that with respect to baseline Pd/Pa, together adenosine and the contrast medium produced significant hyperemia and decreased hyperemic Pd/Pa values (FFRad and FFRcont). No significant differences between FFR.ad and FFRcont values were found ($p = 0.108$) and significant positive correlation between FFRad and FFRcont was detected ($r = 0.886$ and $p < 0.001$) (29). Table below illustrates aforementioned points in Selim's study.

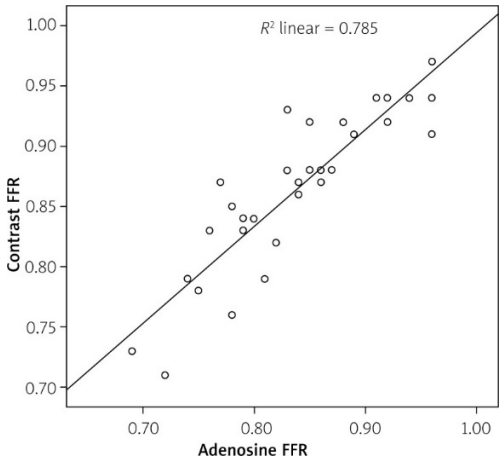

Figure 1.Correlation Plot Between Adenosine and Contrast

Adapted from "Efficacy of coronary fractional flow reserve using contrast medium compared to adenosine (29).

In another study conducted by Bapista and Colleagues (2013), they examined function of Contrast-induced hyperemia in the functional evaluation of coronary lesions with a pressure wire. In their study, FFRcont<0.80 presented a sensibility of 100%, specificity 88%, PPV 78% and NPV 100% for the spotting the lesions with FFRad<0.80. All lesions with a FFRcont>0.84 (n=24, 41.1%) maintained a FFRad≥0.80. Finally, they concluded that the functional severity of lesions was correctly assessed via FFRcont in 72% of cases (37). In consistent with the result of our study Leone and Colleague (2015), postulated that contrast FFR is considered as reliable approach in predicting the functional significance of coronary stenosis (36).

Nowadays, various studies have been conducted so far in assessment of FFRcont; some of these studies discuss FFRcont as reliable, cheap, time saving and practical method, which can generate adequate hyperemia in assessment of hemodynamic importance of coronary stenosis (31, 32, 33).

In the past it was proposed that FFRcont may induce submaximal hyperemia (34), nonetheless now it is substantiated by various literatures that FFRcont induces efficient adequate hyperemia and could be used in the assessment of intermediate coronary stenosis (35, 36).

All in all, it appears plausible that according to aforementioned study and confirming clinical relevance of FFRcont and its applicability, accessibility and budget friendly nature, it can be used as alternative method over FFR via adenosine.

REFERENCES

1. Roger VL. Epidemiology of myocardial infarction. Med Clin North Am 2007; 91:537-52; ix. 10.1016/j.mcna.2007.03.007 [PMC free article] [PubMed] [Cross Ref]
2. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation2008;117:e25-146. 10.1161/CIRCULATIONAHA.107.187998 [PubMed] [Cross Ref]
3. Lloyd-Jones D, Adams RJ, Brown TM, et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation 2010; 121:948-54.

10.1161/CIRCULATIONAHA.109.192666 [PubMed] [Cross Ref]
4. Nichols M, Townsend N, Scarborough P, et al. Cardiovascular disease in Europe 2014: epidemiological update. Eur Heart J 2014; 35:2929. 10.1093/eurheartj/ehu378 [PubMed] [Cross Ref]
5. David Corcoran,1,2 Barry Hennigan,1,2 and Colin Berry corresponding author1,2. (2017). Fractional flow reserve: a clinical perspective. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5489582/. Last accessed August-2017.
6. Eiman Jahangir, MD, FACC Cardiologist Eiman Jahangir, MD, FACC is a member of the following medical societies: American College of Cardiology, American Heart Association. (2016). Fractional Flow Reserve Measurement. Available: http://emedicine.medscape.com/article/1839601-overview. Last accessed August-2017.
7. Pijls NH, van Son JA, Kirkeeide RL, De Bruyne B, Gould KL. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation. 1993; 87:1354–1367. [PubMed]
8. De Bruyne B, Baudhuin T, Melin JA, et al. Coronary flow reserve calculated from pressure measurements in humans: validation with positron emission tomography. Circulation. 1994; 89:1013–1022. [PubMed]
9. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N Engl J Med. 1996; 334:1703–1708. [PubMed]
10. Pijls NH, van Schaardenburgh P, Manoharan G, et al. Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study. J Am Coll Cardiol. 2007; 49:2105–2111. [PubMed]
11. Bech GJ, Droste H, Pijls NH, et al. Value of fractional flow reserve in making decisions about bypass surgery for equivocal left main coronary artery disease. Heart. 2001; 86:547–552. [PMC free article][PubMed]
12. Lindstaedt M, Yazar A, Germing A, et al. Clinical outcome in patients with intermediate or equivocal left main coronary artery disease after deferral of surgical revascularization on the basis of fractional flow reserve measurements. Am Heart J. 2006; 152:156.e1–156.e9. [PubMed]
13. Potvin JM, Rodés-Cabau J, Bertrand OF, et al. Usefulness of fractional flow reserve measurements to defer revascularization in patients with stable or unstable angina pectoris, non-ST-elevation and ST-elevation acute myocardial infarction, or atypical chest pain. Am J Cardiol. 2006; 98:289–297. [PubMed]
14. Fischer JJ, Wang XQ, Samady H, et al. Outcome of patients with acute coronary syndromes and moderate coronary lesions undergoing deferral of revascularization based on fractional flow reserve assessment. Catheter Cardiovasc Interv. 2006; 68:544–548. [PubMed]
15. Berger A, Botman KJ, MacCarthy PA, et al. Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary intervention in patients with multivessel disease. J Am Coll Cardiol. 2005; 46:438–442. [PubMed]
16. Wongpraparut N, Yalamanchili V, Pasnoori V, et al. Thirty-month outcome after fractional flow reserve-guided versus conventional multivessel percutaneous coronary intervention. Am J Cardiol. 2005; 96:877–884. [PubMed]
17. Yohanes Adiputra and Shao-Liang Chen. (2015). Clinical Relevance of Coronary Fractional Flow Reserve: Art-of-state. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4830323/. Last accessed August-2017.
18. Di Segni E, Higano ST, Rihal CS, Holmes DR, Jr, Lennon R, Lerman A. Incremental doses of intracoronary adenosine for the assessment of coronary velocity reserve for clinical decision making. Catheter Cardiovasc Interv. 2001; 54:34–40. [PubMed]
19. De Bruyne B, Pijls NH, Barbato E, Bartunek J, Bech JW, Wijns W, et al. Intracoronary and intravenous adenosine 5'-triphosphate, adenosine, papaverine, and contrast medium to assess fractional flow reserve in humans. Circulation. 2003; 107:1877–83. [PubMed]
20. Sonoda S, Takeuchi M, Nakashima Y, Kuroiwa A. Safety and optimal dose of intracoronary adenosine 5'-triphosphate for the measurement of coronary flow reserve. Am Heart J. 1998; 135:621–7. [PubMed]

21. Jeremias A, Filardo SD, Whitbourn RJ, Kernoff RS, Yeung AC, Fitzgerald PJ, et al. Effects of intravenous and intracoronary adenosine 5'-triphosphate as compared with adenosine on coronary flow and pressure dynamics. Circulation. 2000; 101:318–23. [PubMed]
22. Topol EJ, and Nissen SE: Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995; 92: pp. 2333-2342 (tel:2333-2342) Cross Ref (http://dx.doi.org/10.1161/01.CIR.92.8.2333)
23. Meijboom WB, Van Mieghem CAG, van Pelt N, et al: Comprehensiveassessment of coronary artery stenoses: computed tomography coronaryangiography versus conventional coronary angiography and correlation with angiography versus conventional coronary angiography and correlation with fractional flow reserve in patients with stable angina. J Am Coll Cardiol 2008; 52: pp. 636-643 Cross Ref (http://dx.doi.org/10.1016/j.jacc.2008.05.024)
24. Ziaee A, Parham WA, Herrmann SC, et al: Lack of relation between imaging and physiology in ostial coronary artery narrowings. Am J Cardiol 2004; 93: pp. 1404-1407 Cross Ref (http://dx.doi.org/10.1016/j.amjcard.2004.02.041)
25. Morton J. Kern (2015). Cardiovascular Intervention: A Companion to Braunwald's Heart Disease,. United Kingdom: Elsevier. 230.
26. Jeremias A, Whitbourn RJ, Filardo SD, et al: Adequacy of intracoronary versus IV adenosine-induced maximal coronary hyperemia for fractional flow reserve measurements. Am Heart J 2000; 140: pp. 651-657Cross Ref (http://dx.doi.org/10.1067/mhj.2000.109920)
27. Casella G, Leibig M, Schiele TM, et al: Are high doses of intracoronaryadenosine an alternative to standard intravenous adenosine for the assessmentof fractional flow reserve? Am Heart J 2004; 148: pp. 590-595 Cross Ref (http://dx.doi.org/10.1016/j.ahj.2004.04.008)
28. Nobuo Shiode,1 Tomokazu Okimoto,2 Hiromichi Tamekiyo,2 Tomoharu Kawase,2 Kenichi Yamane,2 Yuzo Kagawa,2 Yuto Fujii,2 Yusuke Ueda,2 Naoya Hironobe,2 Yasuko Kato,2 and Yasuhiko Hayashi2. (2017). Contrast-induced Hyperemia as an Alternative to Drug-induced Hyperemia in the Evaluation of the Fractional Flow Reserve in Coronary Lesions. Available: http://pubmedcentralcanada.ca/pmcc/articles/PMC5348447/. Last accessed August-2017.
29. Selim Topcu,corresponding author1 Ibrahim Halil Tanboğa,1 Enbiya Aksakal,1 Uğur Aksu,2 Oktay Gulcu,1 Oğuzhan Birdal,1 Arif Arısoy,1 Arzu Kalaycı,3 Fatih Rifat Ulusoy,4 and Serdar Sevimli1. (2016). Efficacy of coronary fractional flow reserve using contrast medium compared to adenosine. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5011536/. Last accessed August-2017.
30. Berry C, van 't Veer M, Witt N, et al. VERIFY (VERification of Instantaneous Wave-Free Ratio and Fractional Flow Reserve for the Assessment of Coronary Artery Stenosis Severity in EverydaY Practice): a multicenter study in consecutive patients. J Am Coll Cardiol. 2013;61:1421–7. [PubMed]
31. Hernández F1, Mora L, García-Tejada J, Velázquez M, Gómez-Blázquez I, Bastante T, Albarrán A, Andreu J, Tascón J.. (2009). Comparison of iodixanol and ioversol for the prevention of contrast-induced nephropathy in diabetic patients after coronary angiography or angioplasty. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5011536/. Last accessed August-2017.
32. McGeoch RJ, Oldroyd KG. Pharmacological options for inducing maximal hyperaemia during studies of coronary physiology. Catheter Cardiovasc Interv. 2008; 71:198–204. [PubMed]
33. Tatineni S, Kern MJ, Deligonul U, et al. The effects of ionic and nonionic radiographic contrast media on coronary hyperemia in patients during coronary angiography. Am Heart J. 1992; 123:621–7. [PubMed]
34. Tatineni S, Kern MJ, Deligonul U, et al. The effects of ionic and nonionic radiographic contrast media on coronary hyperemia in patients during coronary angiography. Am Heart J. 1992; 123:621–7. [PubMed]
35. Kanaji Y, Murai T, Lee T, et al. Efficacy of pressure parameters obtained during contrast medium-induced submaximal hyperemia in the functional assessment of intermediate coronary stenosis. Int J Cardiol. 2016; 202:207–13. [PubMed]
36. Leone AM, Scalone G, De Maria GL, et al. Efficacy of contrast medium induced Pd/Pa ratio in predicting functional significance of intermediate coronary artery stenosis assessed by fractional flow reserve: insights

from the , study. EuroIntervention. 2015; 11:421–7. [PubMed]

37. S.B. Baptista J. Loureiro L. Brizida P. Magno P. Leal E. Lourenco C. Monteiro M. Nedio P. Farto E Abreu V. Gil. (2013). Contrast-induced hyperemia in the functional evaluation of coronary lesions with a pressure wire. Available: https://academic.oup.com/eurheartj/article/2862123. Last accessed Sep2017.