Health Technology Assessment in India

Effectiveness of FFR Vs. Angiography Guided PCI in Patients with Stable Coronary Artery Disease

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SUMMARY

We evaluated and compiled the existing evidence regarding the clinical effectiveness of Fractional Flow Reserve (FFR) guided Percutaneous Coronary Intervention (PCI) in comparison to angiography guided PCI in stable coronary artery disease (CAD) patients with intermediate stenosis (50-70%), alongside the cost implications of using FFR on intermediate stenosis patients referred to undergo PCI. Long-term clinical outcomes including major adverse cardiac events (MACEs), mortality, and myocardial events (MI), were reported to be comparable between FFR-guided and angiography-guided PCI. Studies suggested FFR reduces number of unnecessary PCIs in intermediate stenosis by measuring the physiological significance of the coronary lesions. However, data on the actual reduction in PCIs using FFR in clinical practice in India was unavailable. A cost-minimization analysis indicated no savings upon using FFR in stable CAD at current FFR wire and stent prices. Potential for savings may emerge if the cost of the FFR wire substantially decreases compared to the stent cost. It is crucial to evaluate how integrating FFR into routine practice may impact the number of deployed stents, before conducting a cost-effectiveness analysis.

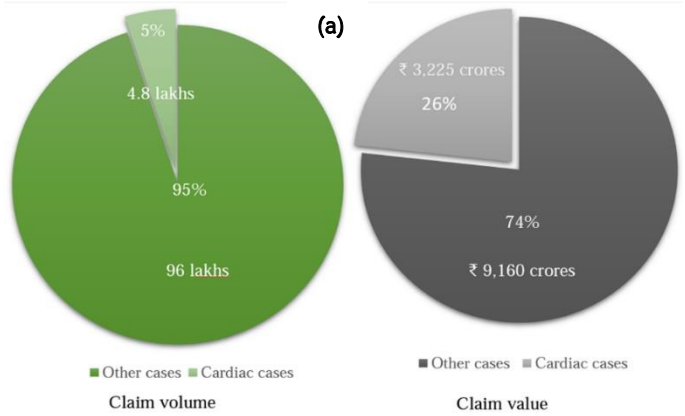
BACKGROUND

Fractional Flow Reserve (FFR) is a test that measures the coronary artery pressures distal (Pd) and proximal (Pa) to the stenosis (Fig. 1) providing more accurate information of ischemia in coronary artery disease, especially in cases of intermediate severity (50%-70%). Coronary lesions with an FFR value greater than 0.80 have been reported to be managed safely without the need for revascularization.

The global strategy for Acute Coronary Syndrome is widely accepted, but challenges arise in judiciously using PCI and Stenting for stable CAD. 2018 National Interventional Council (NIC) data indicated there were 438,351 PCIs conducted across 709 centers utilizing 578,164 coronary stents (13.14% increase from the previous year). Drug eluting stents (DES) accounted for 98.12% of stents, 48.81% domestically manufactured (1). Furthermore, an analysis of healthcare utilization trends within the Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB-PMJAY) revealed that cardiac care constituting 5% (4.8 lakhs claims) of the total claims submitted, contributing to 26% (32,235 crores) of the scheme's overall financial expenditure (Fig. 2). Within 130 cardiac packages offered by PM-JAY, the five most frequently availed packages accounted for 70% of the total cardiac care utilization.

Figure 1: Schematic diagram of FFR Wire and measuring coronary artery pressures distal (Pd) and proximal (Pa) to the stenosis (3)

And amongst those top five packages, PTCA-Single stent procedure held the highest utilization rate at 34%, followed closely by PTCA-Double stent at 29% (Fig. 2) (2).



Procedure Name	Percentage
PTCA-Single Stent	34%
PTCA-Double Stent	20%
CABG	9%
Management of Acute MI	4%
Mitral Valve Replacement	3%
Atrial Septal Defect (ASD)	2%
IABP	2%
Others	26%

Claim volume

Procedure Name	Percentage
PTCA-Single Stent	32%
PTCA-Double Stent	24%
CABG	13%
Mitral Valve Replacement	5%
Atrial Septal Defect (ASD)	2%
Management of Acute MI	2%
Double valve replacement	1%
Others	19%

Claim value

Figure 2: (a) Claim volume vs claim value across India (b) Top cardiac packages.

The rising trend in PCI and stent package utilization in India highlights the necessity for effective strategies to accurately diagnose ischemia and optimize PCIs and stenting in stable CAD patients. Currently, coronary angiography is recommended as a diagnostic tool for stable CAD patients with high-risk clinical conditions, guiding revascularization decisions (4). However, angiography is reported to have limitations, especially in intermediate-severity stenoses (40–70%), accurately predicting functional significance in less than 50% of cases (5). Therefore, decisions for revascularization in intermediate coronary lesions (50-70% stenosis) are recommended to be based on physiological significance of coronary lesions. Fractional Flow Reserve (FFR) has been reported to provide more precise information about the physiological significance of coronary lesions, especially in cases stable CAD of intermediate severity (50%-70%), leading to more informed clinical decisions and tailored treatment depending upon the patients need (6-9).

This study compared FFR-guided PCI to angiography-guided PCI in stable coronary artery disease patients with 50-70% stenosis. It aimed to assess clinical effectiveness and cost implications of FFR use.

METHODOLOGY

1. For the clinical effectiveness comparison, a rapid literature review was conducted that included evaluating the systematic reviews, meta-analyses, and clinical trials, focusing on outcomes such as major Adverse Cardiac Events (MACE), Myocardial Infarction (MI), Cardiovascular Mortality (CM), All-Cause Mortality (ACM), Revascularization (RV), stent thrombosis, and major bleeding. Specific inclusion and exclusion criteria were applied to select relevant studies, and data were sourced from PubMed, including MEDLINE, and the Cochrane Library.
2. For the cost implications evaluation, a similar rapid review was conducted, specifically targeting Indian studies reporting FFR-guided revascularization costs.
3. Furthermore, a costing analysis was also undertaken using assumptions from the literature.
4. Clinician's opinions were also gathered with the help of a questionnaire and online communication, from interventional cardiologists from the government medical hospitals as well as private hospitals, on the use of FFR.

RESULTS

1. Search Results

For the clinical effectiveness comparison out of total 440 studies retrieved (PubMed - 126 and Cochrane - 314) 13 articles were found to be eligible for data extraction. Similarly, for cost implications out of 13 articles only two were found to be eligible for data extraction (Fig. 3).

Information was collected from the chosen studies with the help of a Data Extraction Table. Subsequently, a comprehensive narrative data synthesis was performed based on the gathered information.

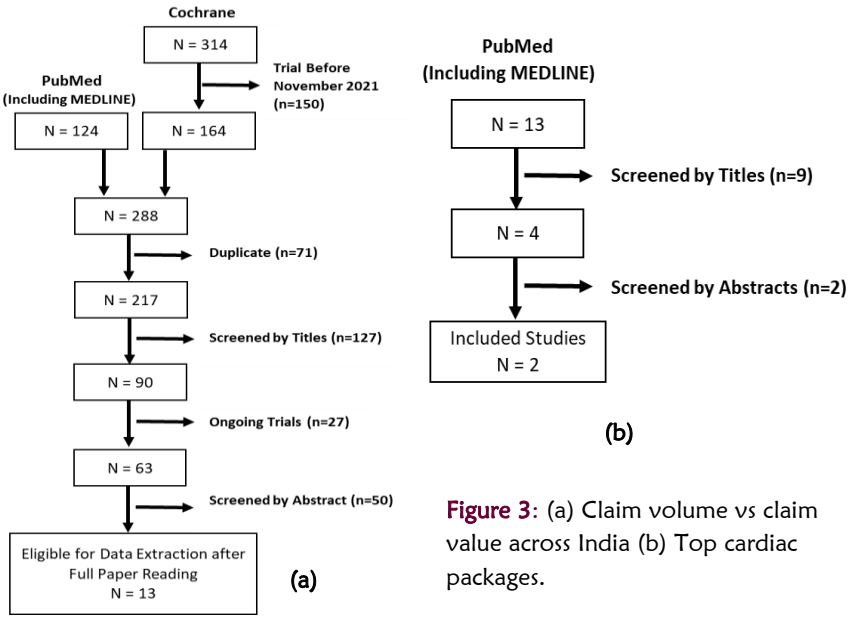


Figure 3: (a) Claim volume vs claim value across India (b) Top cardiac packages.

2. Data Synthesis

I. Clinical- Effectiveness

(a) Major Adverse Cardiovascular Events (MACE)

No significant difference was found in long-term MACE between FFR-guided and angiography-guided PCI in patients with obstructive CAD. Seven studies reported no significant difference in MACE between the two approaches, with odds ratios (OR) ranging from 0.86 to 1.02 and relative risk (RR) close to 1. One study suggested a trend towards reduced in-hospital MACE (OR 0.63) and one on follow-up (OR 0.83) with FFR-guided PCI.

(b) Myocardial Infarction (MI)

No significant difference found in the reduction of MI between FFR-guided and angiography-guided PCI groups across various patient cohorts (chronic coronary syndrome, obstructive CAD, and multi-vessel CAD (OR 0.6 - 1 and RR close to 1. Some studies reported insignificant reductions in MI with FFR-guided PCI (OR close to 0.74, 95% CI 0.49–1.10).

(c) Cardiovascular Mortality

No significant difference in cardiovascular mortality was reported between FFR - and angiography-guided revascularization in patients with stable CAD suggesting similar outcomes with both approaches.

(d) All-Cause Mortality

No significant impact of FFR guided PCI and angiography-guided PCI strategies was indicated on all-cause mortality in patients with Chronic Coronary Syndrome (CCS) without LM disease or reduced left ventricle ejection fraction (LVEF), obstructive CAD, and multi-vessel CAD (RR close to 1). Similarly, no significant differences were reported in in-hospital or follow-up all-cause mortality. While few studies suggested potential reductions in risk of all-cause mortality with FFR-guided PCI (though insignificant).

(e) Revascularization

FFR-guided approaches showed reduced revascularization rates and lower in-hospital target lesion revascularization (TLR) compared to angiography. However, no significant differences were reported in repeat revascularization rates or unplanned revascularization between FFR-guided and angiography-guided strategies over time.

(f) Number of PCIs, Stents Placed and Stent-Thrombosis

FFR-guided revascularization resulted in decreased number of PCIs performed and fewer number of stents placed compared to angiography-guided procedures. This was supported by findings indicating that lesions initially deemed significant by angiography were reclassified as not physiologically significant by FFR, leading to a reduction in the average number of stents used in FFR-guided interventions. Additionally, no significant difference was reported in stent thrombosis rates between FFR and angiography-guided procedures.

(g) Management Strategies, Hospitalization Cost and Procedural Details

98% of patients with angiography + FFR had clear management plans compared to 15% in the angiography-only group (RIPCORD-2 Trial). While FFR-PCI showed lower mean procedure costs due to stable procedure time, total costs remained similar. Hospital stays and outpatient visits were comparable. Procedural duration and contrast agent volume didn't significantly differ across studies, but RIPCORD 2 reported longer duration and increased contrast/radiation use with FFR.

(h) Quality of Life (QoL)

No significant difference in quality-of-life (QoL) between the angiography-only and angiography + FFR groups, as measured by the EuroQol EQ-5D-5L visual analog scale. However, RIPCORD 2 suggested that FFR may improve QoL in patients with more severe disease.

III. Cost-Implications of using FFR and Clinical Outcomes - Indian Context

Existing evidence focusing on the costing of the FFR strategy, especially in the Indian context, was compiled. Only two Indian studies addressed the costing of FFR in addition to clinical outcomes.

(a) Stent Avoidance, Stent Reduction and Change in Revascularization Decision:

Study conducted at CMC Vellore observed that FFR-guided strategy resulted in 30% stent avoidance and 31% stents reduction, shifting 10% patients from CABG to multi-vessel PCI, and 8.25% patients from PCI to CABG. A similar trend was observed in an earlier FIND study (38% reduction in stent usage).

(b) Clinical Outcomes

i. **Primary Endpoints:** The composite primary endpoint (cardiac death, non-fatal myocardial infarction (MI), ischemia, or ischemia-driven revascularization in the assessed vessel) were significantly lower in the stent avoidance group compared to the combined stented group (0.9% vs. 6.9%, p = .04; 95% CI: −0.10 to −0.10).

ii. **Secondary Endpoints:** Extended MACE (death, nonfatal myocardial infarction, and ischemia-driven revascularization) showed no statistically significant difference (p = .29) between the avoided and stented groups. Adverse events related to adenosine were minimal, with no significant difference between intracoronary and intravenous administration.

iii. **Micro-Costing of FFR:** Considering an average Stent Cost of Rs. 46,753 (Range: Rs. 25,000 to Rs. 1,40,000) and FFR wire cost as Rs. 21,200, re-used on average two patients the FFR strategy led to per-patient savings of INR 51,847 and total savings of INR 15,813,379 (305 patients). Considering 2019 Stent Cost of 30,080 and revised FFR wire cost of Rs. 30,000 three pricing scenarios explored (representing public and private settings) showing FFR as a cost-saving strategy (per-patient savings ranging from Rs. 4,531 to Rs. 32,515). An earlier FIND study also highlighted FFR strategy as cost-saving with a net saving of INR 8,57,600 in one year, including savings from avoiding Dual Antiplatelet Therapy (DAPT) costs for stented patients. considering Stent Cost as Rs. 1 lakh and FFR procedure cost as Rs. 30,000.

II. Costing

Costing of FFR strategy was conducted based on assumptions that **FFR resulted in stent avoidance in 30% of cases, stent reduction in 30%,** and **no change in decision in 40% of patients** with intermediate lesions. **Prevalence of multi-vessel CAD set at 30%** with **2 lesions per patient**, Considering the current **stent cost of Rs. 38,265** and **FFR wire costs of Rs. 40,000**, **FFR strategy didn't show immediate cost savings**. Nonetheless, it could potentially be cost saving if the FFR wire cost was below INR 17,500 (for single use) or INR 35,000 (for reuse on two patients after sterilization). Incorporating variations in procedure costs and guide wire use could provide a more realistic assessment of FFR's cost relative to stent cost.

IV. Clinician's Opinion

Responses from six interventional cardiologists, with 4 to 22 years of experience and consultations ranging from 500 to 1200 patients per month, were collected. All respondents **highlighted the positive aspects of FFR**, recognizing its role in assessing lesion significance and guiding revascularization decisions, especially in cases of intermediate coronary stenosis and complex lesions. FFR's utility in decision-making for bifurcation lesions was also noted. FFR was seen as an alternative to the non-invasive tests (trade-mill testing/ dobutamine stress testing etc.) to provide evidence of Ischemia, if former methods were inconclusive. Regarding FFR costs, a range from INR 30,000 to INR 70,000 were cited, with suggestions to explore advanced techniques like CT-FFR, iFR, and RFR. However, the survey revealed that FFR wasn't routinely incorporated into routine practice in three out of the six represented hospitals.

Conclusions

In summary, FFR-guided and angiography-guided PCI showed similar clinical outcomes in stable CAD patients with intermediate stenoses (50-70%). While FFR has potential to reduce PCIs, actual data on avoided procedures are lacking. Understanding FFR's impact on stent deployment is crucial before cost-effectiveness analysis. Limited Indian studies prompt comprehensive costing assessments. FFR's potential cost-saving hinges on wire cost versus stents. Integrating FFR into practice requires evaluation of its potential impact on number of deployed stents before conducting a cost-effective analysis.

Recommendations

The potential impact of incorporating FFR into routine practice needs evaluation to assess its effect on the number of deployed stents in Indian context before conducting a cost-effectiveness analysis.

Limitations

i. *The study used a rapid review for assessing FFR's clinical effectiveness and cost implications.*
ii. *Costing analysis was based upon some preliminary assumptions from the literature.*

References

1. *Arramraju SK, Janapati RK, Sanjeeva Kumar E, Mandala GR. National interventional council data for the year 2018-India. Indian Heart J. 2020;72(5):351–5.*
2. *Sehgal, K. P.; Chandrashekhar, S.; Naib P. Trends in Cardiac Care utilisation under Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (PM-JAY). 2021. Available from: https://pmjay.gov.in/sites/default/files/2021-06/Analysis-of-Cardiac-Packages-Utilization-Under-PMJAY_Final.pdf*
3. *Picture Courtesy: https://www.sozocardiology.com/heart-treatments/fractional-flow-reserve-ffr-study/*
4. *Balanescu S. Fractional Flow Reserve Assessment of Coronary Artery Stenosis. Eur Cardiol Rev [Internet]. 2016;11(2):77–82.*
5. *Chowdhury M, Osborn EA. Physiological Assessment of Coronary Lesions in 2020. Curr Treat Options Cardiovasc Med [Internet]. 2020 Jan 15;22(1):2.*
6. *Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the. Circulation [Internet]. 2012 Dec 18;126(25):e354-471.*
7. *Tebaldi M, Campo G, Biscaglia S. Fractional flow reserve: Current applications and overview of the available data. World J Clin cases [Internet]. 2015 Aug 16;3(8):678–81.*
8. *Panchal HB, Veeranki SP, Bhatheja S, Barry N, Mahmud E, Budoff M, et al. Fractional flow reserve using computed tomography for assessing coronary artery disease: a meta-analysis. J Cardiovasc Med (Hagerstown). 2016 Sep;17(9):694–700.*
9. *Balanescu S. Fractional Flow Reserve Assessment of Coronary Artery Stenosis. Eur Cardiol Rev [Internet]. 2016;11(2):77–82.*