International Journal of Cardiology 344 (2021) 54–59

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Instantaneous wave-free ratio compared with fractional flow reserve in PCI: A cost-minimization analysis

Karolina Berntorp [a,1], Josefine Persson [b,1], Sasha M. Koul [a,1], Manesh R. Patel [c,1], Evald H. Christiansen [d,1], Ingibjörg Gudmundsdottir [e,1], Troels Yndigegn [a,1], Elmir Omerovic [f,1], David Erlinge [a,1], Ole Fröbert [g,1], Matthias Götberg [a,*,1]

[a] Department of Cardiology, Lund University, Skåne University Hospital, Lund, Sweden
[b] School of Public Health and Community Medicine, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden
[c] Duke University, Durham, NC, United States
[d] Department of Cardiology, Aarhus University Hospital, Skejby, Denmark
[e] Department of Cardiology, Reykjavik University Hospital and University of Iceland, Reykjavik, Iceland
[f] Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden
[g] Örebro University, Faculty of Health, Department of Cardiology, Örebro, Sweden

ARTICLE INFO

Keywords:
Instantaneous wave-free ratio
Fractional flow reserve
Cost-minimization analysis

ABSTRACT

Background: Coronary physiology is a routine diagnostic tool when assessing whether coronary revascularization is indicated. The iFR-SWEDEHEART trial demonstrated similar clinical outcomes when using instantaneous wave-free ratio (iFR) or fractional flow reserve (FFR) to guide revascularization. The objective of this analysis was to assess a cost-minimization analysis of iFR-guided compared with FFR-guided revascularization.

Methods: In this cost-minimization analysis we used a decision-tree model from a healthcare perspective with a time-horizon of one year to estimate the cost difference between iFR and FFR in a Nordic setting and a United States (US) setting. Treatment pathways and health care utilizations were constructed from the iFR-SWEDEHEART trial. Unit cost for revascularization and myocardial infarction in the Nordic setting and US setting were derived from the Nordic diagnosis-related group versus Medicare cost data. Unit cost of intravenous adenosine administration and cost per stent placed were based on the average costs from the enrolled centers in the iFR-SWEDEHEART trial. Deterministic and probabilistic sensitivity analyses were carried out to test the robustness of the result.

Results: The cost-minimization analysis demonstrated a cost saving per patient of $681 (95% CI: $641 - $723) in the Nordic setting and $1024 (95% CI: $934 - $1114) in the US setting, when using iFR-guided compared with FFR-guided revascularization. The results were not sensitive to changes in uncertain parameters or assumptions.

Conclusions: IFR-guided revascularization is associated with significant savings in cost compared with FFR-guided revascularization.

1. Introduction

Invasive coronary physiology assessment is an established method for determining blood flow limitations when the significance of stenosis is uncertain using angiography alone. Fractional flow reserve (FFR) was the first method to be introduced into clinical practice [1]. FFR is defined as the ratio of the pressure distal to the stenosis to the pressure proximal to the stenosis during maximal hyperemia, usually induced by adenosine. The method carries a class IA classification in clinical guidelines for assessment of intermediate grade stenosis when there is no evidence of ischemia, as it improves clinical outcome compared with medical treatment and revascularization using angiographic assessment alone [2–5]. The extent to which FFR has been implemented into clinical practice is lower than expected [6]. Factors influencing the clinical

* Corresponding author at: Department of Cardiology, Clinical Sciences, Lund University Skåne University Hospital, 222 41 Lund, Sweden.
E-mail addresses: karolina.berntorp@med.lu.se (K. Berntorp), josefine.persson.2@gu.se (J. Persson), sashamkoul@gmail.com (S.M. Koul), manesh.patel0017@gmail.com (M.R. Patel), evald.christiansen@dadlnet.dk (E.H. Christiansen), ig@landspitali.is (I. Gudmundsdottir), troels.yndigegn@gmail.com (T. Yndigegn), elmir@wlab.gu.se (E. Omerovic), david.erlinge@med.lu.se (D. Erlinge), ole.frobert@regionorebrolan.se (O. Fröbert), matthias.gotberg@med.lu.se (M. Götberg).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

https://doi.org/10.1016/j.ijcard.2021.09.054
Received 29 June 2021; Received in revised form 22 September 2021; Accepted 27 September 2021
Available online 30 September 2021

uptake are likely the added time and complexity to the procedure, cost and side effects of adenosine administration, contraindications to adenosine or lack of reimbursement [6,7].

Instantaneous wave-free ratio (iFR) is a diagnostic method similar to FFR, used to assess coronary artery stenosis severity without requiring a hyperaemic agent [8]. IFR was introduced following the establishment of coronary physiology with FFR and a series of comparative validation studies has confirmed the diagnostic accuracy of iFR compared with FFR [8–11]. Today iFR also carries a class IA recommendation in clinical guidelines for assessment of intermediate grade stenosis [5].

In two large clinical trials, iFR-guided revascularization was non-inferior to FFR-guided revascularization concerning clinical outcome [12,13]. The aim of this analysis was to estimate the cost-effectiveness of iFR-guided revascularization compared with FFR-guided revascularization based on the Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Patients with Stable Angina Pectoris or Acute Coronary Syndrome (iFR-SWEDEHEART) trial.

1.1. Summary of the iFR-SWEDEHEART trial

The iFR-SWEDEHEART trial was a multicenter, randomized, controlled, open-label clinical trial. The trial involved fourteen hospitals in Sweden, Denmark and Iceland. The trial was conducted in accordance with the Declaration of Helsinki and was approved by ethical review boards in Sweden, Denmark, and Iceland. All participants provided written informed consent. The one-year results from the trial have previously been published [13].

The main findings were that among patients with stable angina or an acute coronary syndrome, iFR-guided revascularization was non-inferior to FFR-guided revascularization with respect to the rate of major adverse cardiac events (MACE), defined as all-cause mortality, non-fatal myocardial infarction and unplanned revascularization.

A total of 2037 patients were enrolled: 1019 patients in the iFR group and 1018 patients in the FFR group. A primary endpoint event occurred in 6.7% in the iFR group compared with 6.1% in the FFR group (95% confidence interval [CI], −1.5 to 2.8; $P = 0.007$ for non-inferiority; hazard ratio, 1.12; 95% CI, 0.79 to 1.58; $P = 0.53$). In the iFR group numerically fewer revascularizations were performed (536 vs. 569 patients, $P = 0.11$), numerically fewer patients underwent percutaneous coronary intervention (PCI) (443 vs. 456 patients, $P = 0.50$), numerically fewer stents were placed (1.58 ± 1.08 vs. 1.73 ± 1.19, $P = 0.05$) and numerically fewer patients underwent coronary artery bypass grafting (CABG) (93 vs. 113 patients, $P = 0.13$) compared with the FFR group.

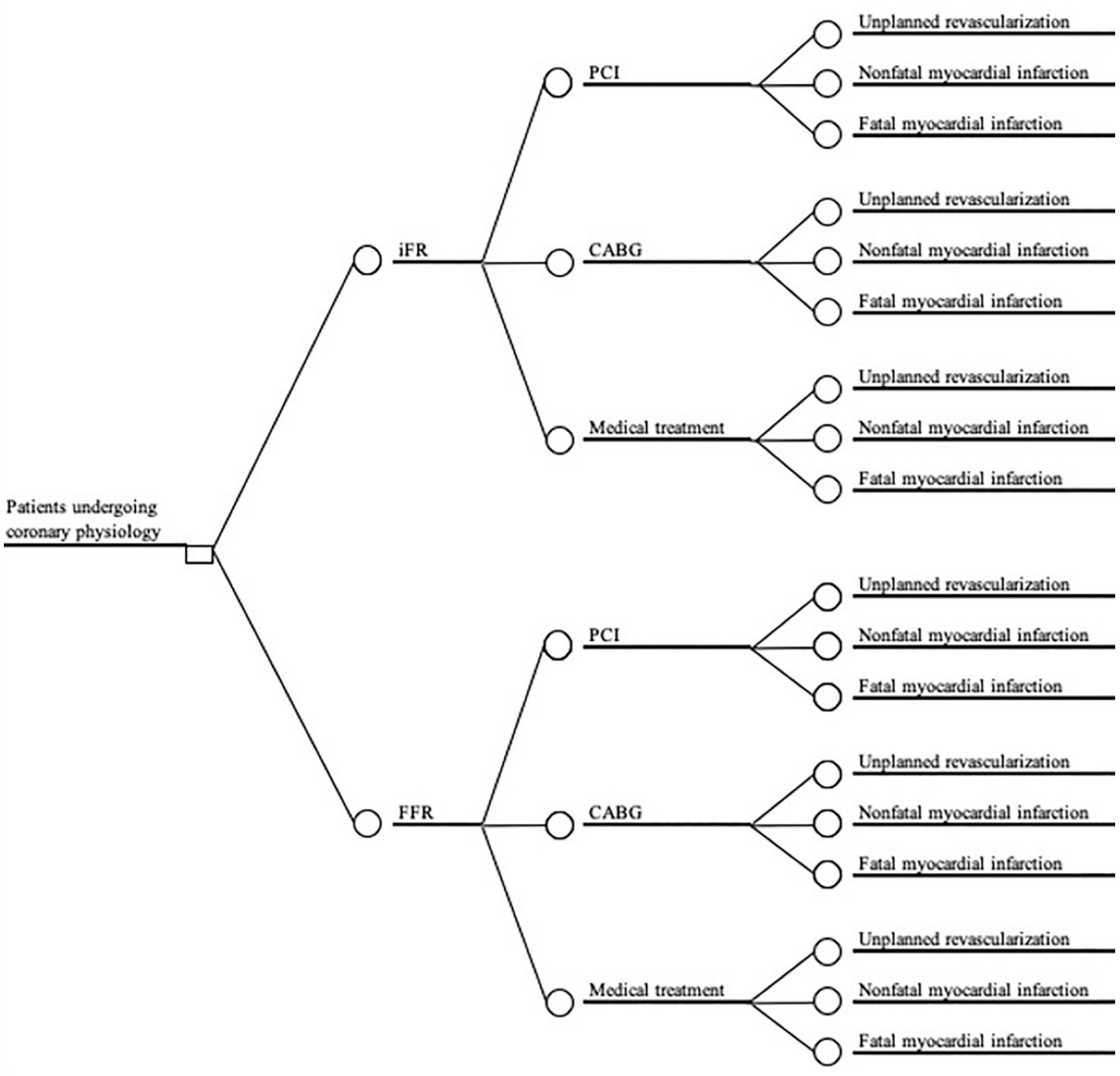

Fig. 1. Decision tree with transition probabilities of Instantaneous wave-free ratio in comparison with Fractional flow reserve for patients undergoing coronary physiology.

2. Methods

2.1. The decision-analytic model

We estimated the cost difference between iFR and FFR in a healthcare perspective over one year by using the published iFR-SWEDEHEART trial data to develop a decision-analytic model [13]. A decision-tree model was designed for a hypothetical cohort of 1000 patients undergoing invasive coronary physiology evaluation (Fig. 1). The model starts with a square node indicating a decision problem between iFR and FFR in patients undergoing coronary physiology. For each decision, the branches of the decision-tree contain probabilities of revascularization with PCI, CABG or medical treatment. For each of these probabilities, there is a risk of unplanned revascularization, nonfatal myocardial infarction and fatal myocardial infarction.

The decision model was applied for a Nordic setting and a United States (US) setting, including relevant costs and probabilities for each scenario. The primary outcome of the model was the cost of each strategy. A cost-minimization analysis was performed due to the proven clinical non-inferiority of iFR compared with FFR to estimate the cost difference [12,13]. No effect data were relevant to include in the model.

The models were programmed in Microsoft Excel (Microsoft, Redmond, WA, USA).

2.2. The resource use and cost data

Cost data for the Nordic setting were derived from Nordic diagnosis-related group (NordDRG) using weights for year 2020 [14]. Due to lack of certain patient specific information of cost utilization during hospital stay the NordDRG codes for uncomplicated conditions were consistently used. Thus, the NordDRG codes for PCI (E19N), CABG (E07E), nonfatal myocardial infarction (E41E) and fatal myocardial infarction (E42N) were used. Cost data for the US setting were estimated from Medicare cost data by Diagnostic Related Group (DRG) code with weights current for year 2020. Included DRG codes were unplanned PCI (246), CABG (232), non-fatal acute myocardial infarction (280), and fatal acute myocardial infarction (283) [15].

The cost of adenosine administration and cost per stent placed were based on the average cost among the participating centers in the iFR-SWEDEHEART trial [13]. The cost of stents placed is included in the NordDRG. The cost in the Nordic setting is presented in US dollars (US$) with an exchange rate of 0.12 from SEK to US$ as per December 16, 2020.

2.3. Sensitivity analysis

Both deterministic and probabilistic sensitivity analyses were carried out to study the uncertainty of parameters and assumptions.

One-way deterministic sensitivity analyses were performed to assess the impact of varying the model cost input, one at the time, while holding other variables fixed at base-case values. Cost per intravenous adenosine administration was varied from minimum to maximum costs for the enrolled centers in the iFR-SWEDEHEART trial [13]. Cost of PCI, CABG, nonfatal myocardial infarction and fatal myocardial infarction, as well as cost per stent placed in the US setting, were varied by 20% around the base-case value. The probability parameters were not tested in the one-way sensitivity analyses due to the similarities in the pathways for the iFR and FFR strategy.

A probabilistic sensitivity analysis of the statistical uncertainty of parameters was undertaken using a Monte Carlo simulation [16]. These parameters included the probabilities and cost for 1000 bootstrap replicates calculating the cost estimates for each simulation. In each simulation, the value for each parameter was sampled from its probability distribution. The probabilities associated with each branch in the pathways were modeled using beta distribution. Since the probabilities associated with each branch are bounded within 0 and 1 (0–100%), a beta distribution is assumed, which does not allow for probabilities outside this range. The parameters of the beta distribution were chosen according to the number of patients observed within each pathway, corresponding to the data from the iFR-SWEDEHEART trial. For the NordDRG cost a uniform distribution was used by varying the cost by 20% around the base-case value. The analyses were programmed in Microsoft Excel (Microsoft, Redmond, WA, US).

3. Results

3.1. Patients

The characteristics of the patients at baseline have previously been published [13]. The mean age was around 67 years and 75% were men. The indication for angiography was stable angina pectoris in 62% of the patients. Approximately 33% had a previous myocardial infarction, 42% had a previous PCI, 22% hade Diabetes Mellitus, 70% had hypertension and 16% were currently smokers.

3.2. Costs

The parameters used in the decision-tree model are presented in Table 1. The probability in the iFR group and FFR group for PCI was 44% vs. 45%, and 9% vs. 11% for CABG. Cost data used for estimation of the cost in the Nordic and US setting are presented in Table 1.

The cost-minimization analyses showed that iFR was cost saving compared to FFR. The cost saving per patient was $681 (95% CI $641 - $723) in the Nordic setting and $1024 ($934 - $1114) in the US setting (Table 2).

3.3. Sensitivity analyses

The one-way sensitivity analyses for the Nordic setting and the US setting showed that the results were not sensitive to major changes in the cost of adenosine administration, PCI, CABG, or the cost per stent placed (US setting). The one-way analyses for each setting are presented as Tornado diagrams (Fig. 2). The reliability of the results was also tested with a probabilistic analysis.

4. Discussion

In this study we used data from the iFR-SWEDEHEART trial to evaluate the health care costs of the use of an iFR-guided revascularization approach compared with FFR. The study demonstrated that iFR-guided revascularization provided significant cost savings compared with FFR-guided revascularization with similar clinical outcomes. Cost savings were driven by a combination of no adenosine administration, a higher rate of safe deferral of revascularization with iFR and therefore a reduced need for revascularization with PCI or CABG at the index procedure.

Coronary physiology guided treatment strategies using FFR were adopted early in clinical practice and the cost-effectiveness of using FFR has been studied in different settings in patients with stable angina pectoris and angiographic intermediate coronary lesions. Without prior functional ischemic testing, FFR-guided revascularization leads to significant cost savings compared with strategies based on myocardial perfusion scan or PCI of all intermediate lesions regardless of whether they are shown to be hemodynamically significant or not [17]. In addition to a favorable clinical outcome, the FAME 2 trial also demonstrated that FFR is cost-effective compared with medical treatment alone in patients with stable coronary artery disease [18].

Despite the evidence supporting the use of FFR for physiological assessment of a coronary artery stenosis as a routine in clinical practice, the uptake has been more limited than expected [6]. There are barriers to FFR with one main issue being the need of achieving maximum hyperaemia, where adenosine is the most commonly used vasodilating

Table 1
Parameters used in the decision-tree model.

Parameters	Value		Distribution
Probabilities iFR[a]			
Iv[b] adenosine administration	0% (0/1012)		Beta
PCI[c]	44% (443/1012)		Beta
CABG[d]	9% (93/1012)		Beta
Unplanned revascularization	5% (47/1012)		Beta
Stents placed per patient (SD[e])	1.58 (±1.08)		Uniform
Nonfatal MI[f]	2% (22/1012)		Beta
Fatal MI[f]	0.2% (2/1012)		Beta
Probabilities FFR[g]			
Iv[b] adenosine administration	100% (1007/1007)		Beta
PCI[c]	45% (458/1007)		Beta
CABG[d]	11% (113/1007)		Beta
Unplanned revascularization	5% (46/1007)		Beta
Stents placed per patient (SD[e])	1.73 (±1.19)		Uniform
Nonfatal MI[f]	2% (17/1007)		Beta
Fatal MI[f]	0.2% (2/1007)		Beta
Costs in Nordic setting (SEK)		Statistics[h]	
Iv[b] adenosine administration	400	110–980	Uniform
PCI[c]	63,131	50,505–75,757	Uniform
CABG[d]	224,113	179,290–268,936	Uniform
Unplanned revascularization	56,370	45,096–67,644	Uniform
Nonfatal MI[f]	33,250	26,600–39,900	Uniform
Fatal myocardial infarction	22,411	17,929–26,893	Uniform
Costs in US setting (US$)		Statistics[h]	
Iv[b] adenosine administration	61	50–73	Uniform
Per stent placed	650	520–780	Uniform
PCI[c]	18,137	14,510–21,764	Uniform
CABG[d]	34,221	27,377–41,065	Uniform
Unplanned revascularization	18,137	14,510–21,764	Uniform
Nonfatal MI[f]	9323	7458–11,188	Uniform
Fatal MI[f]	10,288	8230–12,346	Uniform

[a] iFR = instantaneous wave-free ratio.
[b] Iv = intravenous.
[c] PCI = percutaneous coronary intervention.
[d] CABG = coronary artery bypass grafting.
[e] SD = Standard Deviation.
[f] MI = myocardial infarction.
[g] FFR = fractional flow reserve.
[h] Range ± 20%.

drug. If maximum hyperaemia is not present, the FFR value will be overestimated, and stenosis severity underestimated [1,19–21]. Consequently the method adds costs and time to the procedure. Adenosine also frequently results in chest discomfort and, occasionally, more serious adverse events [22]. The lack of an alternative index may have contributed to the limited adoption of coronary physiology.

The comparable safety and outcomes of iFR and FFR was demonstrated in the iFR-SWEDEHEART trial and also confirmed in The Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularization (DEFINE-FLAIR) trial [12]. Accordingly, both methods are now recommended in clinical guidelines for guiding coronary revascularization in intermediate grade stenosis [5]. The DEFINE-FLAIR trial also demonstrated significantly shorter procedural time with iFR-guided revascularization whilst procedural time did not differ between iFR and FFR in the iFR-SWEDEHEART trial. The direct

Table 2
Results of the cost-minimization analysis with instantaneous wave-free ratio in comparison with fractional flow reserve for patients undergoing coronary physiology. Base-case estimates and 95% confidence intervals (CI) from probabilistic sensitivity analysis.

Option	Cost per patient		Incremental cost saving per patient	
	SEK	US$	SEK	US$
Swedish setting				
iFR[a]	51,934	6232		
95% CI	(51,706–52,169)	(6205–6260)		
FFR[b]	57,269	6913		
95% CI	(57,360–57,868)	(6883–6943)		
Cost saving			5677	681
95% CI			(5342–5965)	(641–723)
US setting				
iFR[a]		13,984		
95% CI		(13,923–14,046)		
FFR[b]		15,008		
95% CI		(14,943–15,074)		
Cost saving				1024
95% CI				(934–1114)

[a] iFR = instantaneous wave-free ratio.
[b] FFR = fractional flow reserve.

comparison of iFR and FFR regarding cost-effectiveness in our study further distinguishes iFR from FFR. A reduction in procedural time is potentially cost saving but it was not a part of this analysis. Further, reduced procedural time could improve the efficacy in the cath-lab when coronary physiology assessment is indicated.

In the iFR-SWEDEHEART trial the higher rate of safe deferral of revascularization with iFR non-significantly reduced the need for revascularization with either PCI or CABG at the index procedure. In our cost-minimization analysis this is one of the main reasons for a reduced cost with iFR-guided revascularization. There were no significant differences in all-cause death, nonfatal myocardial infarction or unplanned revascularization. However, all events were counted and were part of the cost-minimization analysis. Furthermore, the safe deferral of iFR was confirmed in the merged analysis of the DEFINE-FLAIR and the iFR-SWEDEHEART trial. The study included 4486 patients with coronary revascularization deferred in 1117 patients (50%) in the iFR group and 1013 patients (45%) in the FFR group ($p < 0.01$) with similar clinical outcome. In the deferred population, there was no difference between the iFR and FFR groups in the MACE rate (4.12% vs. 4.05%; fully adjusted hazard ratio: 1.13; 95% CI: 0.72 to 1.79; $p = 0.60$) [23]. The results from this study are similar to the economically evaluation of the DEFINE-FLAIR trial, where a significant reduction in revascularization performed with iFR were one of the main reasons for a significant cost saving with iFR [24].

As coronary physiology reaches wider adoption into clinical practice, with both iFR and FFR being equally safe to guide coronary revascularization, evaluating aspects of health economics is important in an economically challenged health care system. Our study demonstrates an additional cost saving with iFR compared with the well-known cost savings of FFR without interfering with clinical outcome. Further the barriers that come along with FFR are completely or partly diminished with iFR. This could hopefully contribute to a wider adoption of coronary physiology in clinical practice. In addition, an important perspective when choosing an iFR approach compared with FFR is that the substantial cost savings in our analysis is approximately the price of the pressure wire itself. In the near future a further reduction in cost is possible with modern pressure wires that can be used as conventional PCI wires when indicated after coronary physiology assessment. These clinical and economic benefits with iFR, without the need of pharmacological hyperaemia, will hopefully contribute to a more widespread

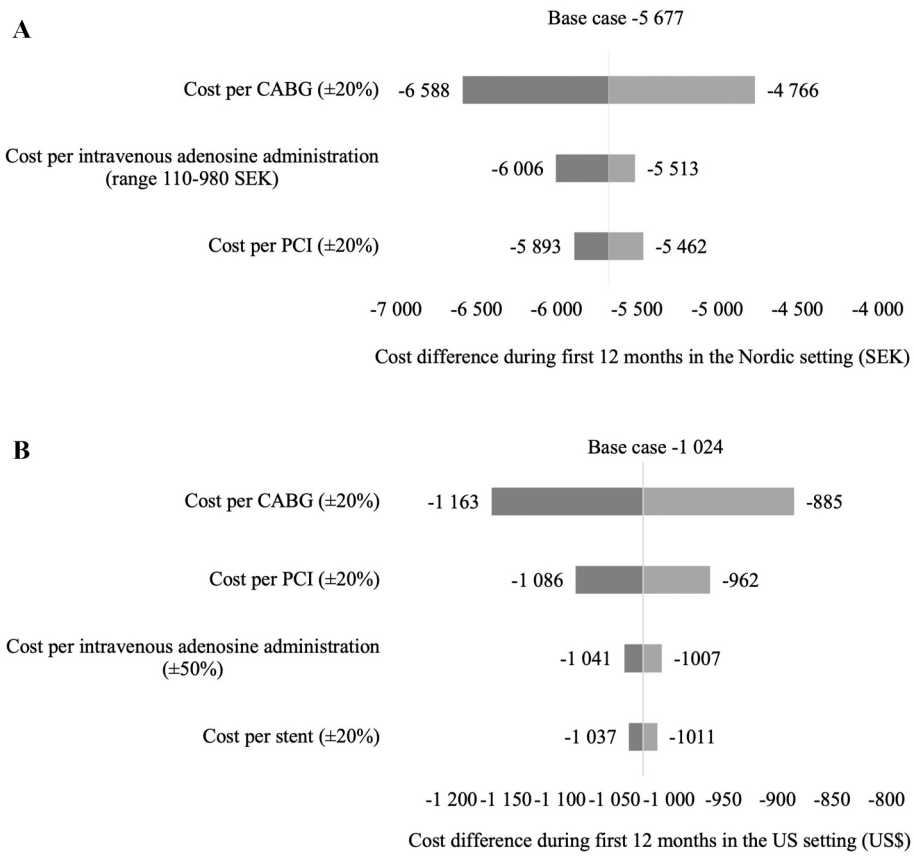

Fig. 2. A & B. Tornado diagrams of the one-way sensitivity analyses representing the most sensitive cost inputs to the output cost difference between Instantaneous wave-free ratio in comparison with Fractional flow reserve for patients undergoing coronary physiology. A represents the Nordic setting, and B represents the US setting. Centre line represents the results from the base-case models.
PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting.

clinical adoption of coronary physiology to guide coronary revascularization.

5. Limitations

This study is based on the one-year results of the iFR-SWEDEHEART trial and long-term cost differences were not assessed. Cost-effectiveness was not a pre-specified endpoint. The calculations were performed on averaged cost for non-complicated treatments or medical conditions such as PCI, CABG, nonfatal myocardial infarction and fatal myocardial infarction due to lack of patient specific information.

6. Conclusions

Based on one-year follow-up data from the iFR-SWEDEHEART trial we demonstrated cost savings with iFR-guided revascularization compared with FFR-guided revascularization. Coronary physiology assessment plays an important role to improve clinical outcome for patients with coronary artery stenosis. The cost savings associated with iFR-guided compared with FFR-guided revascularization, could contribute to an increased adoption of coronary physiology in clinical practice.

Acknowledgement of grant support

The study was funded by an unrestricted research grant from Philips Volcano, which had no role in the design of the trial or the collection, analysis, or reporting of the data.

Declaration of Competing Interest

Dr. Götberg reports receiving lecture fees from Volcano, consulting fees and lecture fees from Boston Scientific, and fees for serving on an advisory board from Medtronic; and Dr. Omerovic, receiving grant support and fees for serving on an advisory board from AstraZeneca and grant support from Abbott. No other potential conflict of interest relevant to this article was reported.

Acknowledgement

None.

References

[1] N.H. Pijls, J.A. van Son, R.L. Kirkeeide, B. De Bruyne, K.L. Gould, 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 87 (4) (1993) 1354–1367.
[2] P.A. Tonino, B. De Bruyne, N.H. Pijls, U. Siebert, F. Ikeno, M. van't Veer, et al., Fractional flow reserve versus angiography for guiding percutaneous coronary intervention, N. Engl. J. Med. 360 (3) (2009) 213–224.
[3] B. De Bruyne, N.H. Pijls, B. Kalesan, E. Barbato, P.A. Tonino, Z. Piroth, et al., Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease, N. Engl. J. Med. 367 (11) (2012) 991–1001.
[4] F.M. Zimmermann, A. Ferrara, N.P. Johnson, L.X. van Nunen, J. Escaned, P. Albertsson, et al., Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial, Eur. Heart J. 36 (45) (2015) 3182–3188.
[5] F.J. Neumann, M. Sousa-Uva, A. Ahlsson, F. Alfonso, A.P. Banning, U. Benedetto, et al., 2018 ESC/EACTS Guidelines on myocardial revascularization, EuroIntervention 14 (14) (2019) 1435–1534.
[6] M. Gotberg, C.M. Cook, S. Sen, S. Nijjer, J. Escaned, J.E. Davies, The evolving future of instantaneous wave-free ratio and fractional flow reserve, J. Am. Coll. Cardiol. 70 (11) (2017) 1379–1402.
[7] N.H. Pijls, P.A. Tonino, The crux of maximum hyperemia: the last remaining barrier for routine use of fractional flow reserve, JACC Cardiovasc. Interv. 4 (10) (2011) 1093–1095.
[8] S. Sen, J. Escaned, I.S. Malik, G.W. Mikhail, R.A. Foale, R. Mila, et al., Development and validation of a new adenosine-independent index of stenosis severity from coronary wave-intensity analysis: results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) study, J. Am. Coll. Cardiol. 59 (15) (2012) 1392–1402.

[9] R. Petraco, J. Escaned, S. Sen, S. Nijjer, K.N. Asrress, M. Echavarria-Pinto, et al., Classification performance of instantaneous wave-free ratio (iFR) and fractional flow reserve in a clinical population of intermediate coronary stenoses: results of the ADVISE registry, EuroIntervention 9 (1) (2013) 91–101.
[10] S. Sen, K.N. Asrress, S. Nijjer, R. Petraco, I.S. Malik, R.A. Foale, et al., Diagnostic classification of the instantaneous wave-free ratio is equivalent to fractional flow reserve and is not improved with adenosine administration. Results of CLARIFY (Classification Accuracy of Pressure-Only Ratios Against Indices Using Flow Study), J. Am. Coll. Cardiol. 61 (13) (2013) 1409–1420.
[11] T.P. van de Hoef, M. Meuwissen, J. Escaned, S. Sen, R. Petraco, M.A. van Lavieren, et al., Head-to-head comparison of basal stenosis resistance index, instantaneous wave-free ratio, and fractional flow reserve: diagnostic accuracy for stenosis-specific myocardial ischaemia, EuroIntervention 11 (8) (2015) 914–925.
[12] J.E. Davies, S. Sen, H.M. Dehbi, R. Al-Lamee, R. Petraco, S.S. Nijjer, et al., Use of the instantaneous wave-free ratio or fractional flow reserve in PCI, N. Engl. J. Med. 376 (19) (2017) 1824–1834.
[13] M. Gotberg, E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, et al., Instantaneous wave-free ratio versus fractional flow reserve to guide PCI, N. Engl. J. Med. 376 (19) (2017) 1813–1823.
[14] Socialstyrelsen, Viktlistor för NordDRG [Updated 9 November 2020]. Available from: https://www.socialstyrelsen.se/utveckla-verksamhet/e-halsa/klassificering-och-koder/drg/viktlistor/, 2019 (accessed 21 September 2021).
[15] Commission MPA, Hospital acute inpatient services payment system [Updated October 2019]. Available from: http://www.medpac.gov/docs/default-source/payment-basics/medpac_payment_basics_19_hospital_final_v2_sec.pdf?sfvrsn=0, 2019 (accessed 18 September 2021).
[16] A.H. Briggs, A.M. Gray, Handling uncertainty in economic evaluations of healthcare interventions, BMJ 319 (7210) (1999) 635–638.
[17] W.F. Fearon, A.C. Yeung, D.P. Lee, P.G. Yock, P.A. Heidenreich, Cost-effectiveness of measuring fractional flow reserve to guide coronary interventions, Am. Heart J. 145 (5) (2003) 882–887.
[18] W.F. Fearon, T. Nishi, B. De Bruyne, D.B. Boothroyd, E. Barbato, P. Tonino, et al., Clinical outcomes and cost-effectiveness of fractional flow reserve-guided percutaneous coronary intervention in patients with stable coronary artery disease: three-year follow-up of the FAME 2 trial (fractional flow reserve versus angiography for multivessel evaluation), Circulation 137 (5) (2018) 480–487.
[19] B. De Bruyne, N.H. Pijls, E. Barbato, J. Bartunek, J.W. Bech, W. Wijns, et al., Intracoronary and intravenous adenosine 5′-triphosphate, adenosine, papaverine, and contrast medium to assess fractional flow reserve in humans, Circulation 107 (14) (2003) 1877–1883.
[20] N.H. Pijls, Optimum guidance of complex PCI by coronary pressure measurement, Heart 90 (9) (2004) 1085–1093.
[21] N.H. Pijls, B. De Bruyne, K. Peels, P.H. Van Der Voort, H.J. Bonnier, J.K.J. J. Bartunek, et al., Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses, N. Engl. J. Med. 334 (26) (1996) 1703–1708.
[22] H.R. Patel, P. Shah, S. Bajaj, H. Virk, M. Bikkina, F. Shamoon, Intracoronary adenosine-induced ventricular arrhythmias during fractional flow reserve (FFR) measurement: case series and literature review, Cardiovasc. Interv. Ther. 32 (4) (2017) 374–380.
[23] J. Escaned, N. Ryan, H. Mejia-Renteria, C.M. Cook, H.M. Dehbi, E. Alegria-Barrero, et al., Safety of the deferral of coronary revascularization on the basis of instantaneous wave-free ratio and fractional flow reserve measurements in stable coronary artery disease and acute coronary syndromes, JACC Cardiovasc. Interv. 11 (15) (2018) 1437–1449.
[24] C.E. Cox, iFR Cheaper Than FFR Over Trajectory of 1 Year: DEFINE-FLAIR Analysis, Available from: http://www.tctmd.com, 2018.