Fractional Flow Reserve: *Multivessel Coronary Disease and FAME Studies*

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest /arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship Grant/ Research Support:
Grant/ Research Support:
Consulting Fees/Honoraria:
Major Stock Shareholder/Equity Interest:
Royalty Income:
Ownership/Founder:
Salary:
Intellectual Property Rights:

Other Financial Benefit (minor stock options):

<u>Company</u> St. Jude Medical NIH-R01 HL093475 (PI)

Medtronic

NIH-R01 HL093475 (PI)

HeartFlow



Overview:

FAME 1

Substudies

Real World MVD Registry

FAME 2

Substudies

FFR-guided CABG and FAME 3



FAME Trial:





Tonino, et al. New Engl J Med 2009;360:213-24.

	Angio- Guided n = 496	FFR- Guided n = 509	P Value
Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001



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Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Equipment cost (US \$)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05



FAME Study: One Year Outcomes



Tonino, et al. New Engl J Med 2009;360:213-24.



FAME Study: Two Year Outcomes

Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)





Pijls, et al. J Am Coll Cardiol 2010;56:177-184

What happens to deferred lesions?





FAME: Economic Evaluation

Bootstrap Analysis



FFR-guided PCI saved >\$2,000 per patient at one year compared to Angioguided PCI



Circulation 2010;122:2545-50.

Anatomic vs. Functional CAD

Patients with angiographically 3VD (N=115), proportions per number of diseased vessels after assessment by FFR





Tonino, et al. J Am Coll Cardiol 2010;55:2816-21.

Functional SYNTAX Score





Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score

Reclassifies > 30% of cases



Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score

Discriminates Risk for Death/MI





Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

FFR in Acute Coronary Syndromes

Comparison of MACE in FAME patients with and without ACS



Tonino, et al. J Am Coll Cardiol Intv 2011;4:1182-9.

FAME 1 Substudy: FFR and Sex

FFR was significantly higher in women than men in the FAME Trial (0.75±0.18 vs. 0.71±0.17, p=0.001)





Kim HS, et al. J Am Coll Cardiol Intv 2012;5:1037-42

FAME 1 Substudy: FFR and Age

Patients \geq 65 years old had a significantly higher mean FFR across all lesions as compared to patients < 65 years old (0.73 vs. 0.70, p=0.029)



Lim HS, et al. Int J Cardiol 2015; in press.

FAME 1 Substudy: FFR and Age

Despite a different proportion of FFR positive lesions, FFR-guided PCI remained equally beneficial in patients ≥ 65 years old vs. < 65 years old



Lim HS, et al. Int J Cardiol 2015; in press.

Real World FFR Use

2,178 pairs of propensity matched patients before and after routine FFR use



Three-vessel disease

Park SJ, et al. Eur Heart J 2013;34:3353-61.

Real World FFR Use

2,178 pairs of propensity matched patients before and after routine FFR use

Repeat revascularization



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Park SJ, et al. Eur Heart J 2013;34:3353-61.

Real World FFR Use

2,178 pairs of propensity matched patients before and after routine FFR use

Death or myocardial infarction





Park SJ, et al. Eur Heart J 2013;34:3353-61.



FAME 2: Two Year Follow-Up

Two year rate of primary endpoint: Death, MI, Urgent Revascularization



De Bruyne, et al. NEJM 2014;371:1208-17.



FAME 2: Two Year Follow-Up

Two year rate of primary endpoint: Death, MI, Urgent Revascularization

Medical Thera (N=441)	apy Hazard Ratio (95% Cl)†	P Value <u>:</u>
no. (%)		
.) 86 (19.5)	0.39 (0.26–0.57)	<0.001
) 8 (1.8)	0.74 (0.26–2.14)	0.58
30 (6.8)	0.85 (0.50–1.45)	0.56
) 72 (16.3)	0.23 (0.14–0.38)	<0.001
b) 36 (8.2)	0.79 (0.49–1.29)	0.35
	Medical Theration 47) (N = 441) no. (%) 1) 86 (19.5) 3) 8 (1.8) 30 6.8) 30 6.8) 5) 36 (8.2)	Medical Therapy (N = 441)Hazard Ratio (95% CI) $\dot{\uparrow}$ 47)No. (%)No. (%)86 (19.5)0.39 (0.26-0.57)308 (1.8)0.74 (0.26-2.14)30 (6.8)0.85 (0.50-1.45)0)72 (16.3)0.23 (0.14-0.38)36 (8.2)0.79 (0.49-1.29)

51% of all urgent revascularizations were due to MI or ischemic ECG

>80% of all urgent revascularizations were due to MI, ischemic ECG, or rest angina



De Bruyne, et al. NEJM 2014;371:1208-17.

FAME 2: Two Year Follow-Up

Landmark Analysis of Death/MI after 7 days







Spontaneous vs. Procedural MI

5 year F/U in 5,467 patients from RITA-3, ICTUS, and FRISC-II





Damman, et al. Circulation 2012;125:568-576.

FAME 2: Cost-Effectiveness

The Incremental Cost-Effectiveness Ratio was \$36,000 per QALY



80% of the 10,000 replications were below the \$50,000/QALY willingness-to-pay threshold and 99.5% were below the \$100,000/QALY threshold

Circulation 2013;128:1335-40.



FFR-Guided CABG?

Of 627 consecutive CABG patients, 198 had FFR guidance on at least one lesion



Toth, et al. Circulation 2013;128:1405-1411



FFR-Guided CABG?

Of 627 consecutive CABG patients, 198 had FFR guidance on at least one lesion

MACE-free survival



Toth, et al. Circulation 2013;128:1405-1411

Where do we go from here?





FAME 3 Trial:



Conclusion:

The FAME studies and "real-world" data support the concept that FFR is an indispensable tool for guiding decisions regarding coronary revascularization in patients with MVD which leads to better resource utilization and most importantly improved patient outcomes.

