FFR and CABG

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Conflict of Interest

• Institutional research grants and speaker’s fee from St. Jude Medical and Boston Scientific to Cardiovascular Research Center Aalst
Background

- Revascularisation of intermediate stenosis can be targeted EITHER by angiographic guidance OR (with no documented ischemia at non-invasive stress testing) by angiography plus FFR $\leq 0.80$ (for stenosis < 90%)
Background

• Revascularisation of intermediate stenosis can be targeted EITHER by angiographic guidance OR (with no documented ischemia at non-invasive stress testing) by angiography plus FFR $\leq 0.80$

• Nevertheless, both DEFER and FAME trials excluded patients with left main coronary disease, coronary anatomy unsuitable for PCI, or significant valve disease
Role of FFR in CABG patients

Before CABG

In patients candidate to CABG:

Does it matter an accurate assessment of the stenosis severity?
Coronary disease progression after CABG

Coronary disease progression after CABG

Cosgrove DM, J Thorac Cardiovasc Surg 1981
IMA graft patency and stenosis severity of native vessel

DS < 50% is a strong predictor of IMA occlusion (OR 21.5 [5.2-64.4])

Berger A et al, Circulation 2004
Venous graft patency and stenosis severity of native vessel

Role of FFR in CABG patients

Before CABG

*In patients candidate to CABG:*

*Is an FFR-guided superior to an Angio-guided strategy?*
Functional significance of coronary stenosis and Graft failure

- 164 CABG pts
- Graft failure:
  - 14% arterial
  - 6 venous

Failure of grafts @ 1 year implanted on arteries with non-significant FFR was 3 times higher
Aim

To compare retrospectively the long-term clinical outcome in patients treated with FFR-guided CABG versus patients treated with Angio-guided CABG.
Angio-guided
n=429

FFR-guided
n=198
Clinical endpoints @ 36 months

- **MACE-free survival**: p=0.908
  - Angio-guided: 429, 396, 296, 200
  - FFR-guided: 198, 181, 126, 64

- **TVR-free survival**: p=0.378
  - Angio-guided: 429, 399, 299, 201
  - FFR-guided: 198, 183, 128, 65

- **MI-free survival**: p=0.780
  - Angio-guided: 429, 400, 296, 201
  - FFR-guided: 198, 184, 130, 67

- **Overall survival**: p=0.137
  - Angio-guided: 429, 405, 301, 206
  - FFR-guided: 198, 190, 135, 70

Toth et al. Circulation 2013
CCS II-IV @ 36 months

Toth et al. Circulation 2013
Sub-analysis

Post hoc subanalysis on graft level

- Inclusion criteria
  - From the same patient population, as described above
  - Patients, where angiographic control performed for any reason ($n_{\text{pat}}=160$)
  - Grafts, placed on vessel with intermediate stenosis ($n_{\text{graft}}=234$)

- Endpoint
  - Graft patency at latest follow-up

Toth et al. Circulation 2013
Graft patency @ 36 months

All grafts

Arterial grafts

Toth et al. Circulation 2013
Summary

• FFR-guidance of CABG is associated:
  • lower number of grafts
  • higher rate of off-pump surgery
  • better functional class

• Despite the lower number of grafts there is no excess in events after FFR-guided CABG
Graft Patency After FFR-guided versus Angio-guided CABG: a randomized clinical trial (GRAFFITI trial)

www.clinicaltrial.gov NCT01810224

Principal investigators:
Emanuele Barbato
Bernard De Bruyne
Gabor Toth
Role of FFR in CABG patients

Before CABG

In patients candidate to CABG and AVR:

Is there a role for FFR in this setting?
Pts with aortic stenosis and at least 1 intermediate coronary lesion (50-70%)

<table>
<thead>
<tr>
<th></th>
<th>FFR-guided (n=106)</th>
<th>Angio-guided (n=212)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before FFR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel disease</td>
<td>1.85 ± 0.97</td>
<td>1.80 ± 0.97</td>
<td>n.s</td>
</tr>
<tr>
<td>After FFR</td>
<td>1.48 ± 1.0</td>
<td>1.80 ± 0.97</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Revascularization rate</td>
<td>61%</td>
<td>62%</td>
<td>n.s</td>
</tr>
<tr>
<td>PCI</td>
<td>24%</td>
<td>13%</td>
<td>0.019</td>
</tr>
<tr>
<td>CABG</td>
<td>39%</td>
<td>49%</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Arterial grafts

- FFR-guided: 0.8 ± 0.64
- Angio-guided: 0.75 ± 0.57
- P = n.s

Venous grafts

- FFR-guided: 0.5 ± 0.68
- Angio-guided: 0.73 ± 0.76
- P = 0.05

Di Gioia G and Barbato E; Unpublished data
Role of FFR in CABG patients

Is FFR guidance also viable in bypassed arteries?
How to ... FFR with occluded bypass graft

FFR of the native stenotic vessel is not different from non-CABG setting
How to ... FFR with open bypass graft

FFR of native stenotic vessel reflects the summation of hyperemic flow depending from both by-pass graft and stenotic native coronary artery
Role of FFR in CABG patients

After CABG

Is FFR guidance also viable in bypass grafts?
How to ... FFR with occluded native vessel

Sensor of the pressure wire can be positioned beyond the graft stenosis!
Sensor of the pressure wire should be positioned beyond the graft stenosis and the distal anastomosis!
Resistance in bypass grafts and FFR

\[ \frac{P_d}{P_a} \]

*LITA always implanted on LAD


9th Coronary Physiology in the CathLab Course, Nice 2015
Role of FFR in CABG patients

After CABG

Is FFR-guided PCI better than Angio-guided PCI in bypass grafts?
Aim

To compare retrospectively the long-term clinical outcome in patients undergoing FFR-guided PCI versus contemporary patients undergoing Angio-guided PCI of intermediate stenosis in bypass graft
Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>FFR guided (n = 65)</th>
<th>Angio guided (n = 158)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>69 ± 9.3</td>
<td>71 ± 8.9</td>
<td>.15</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>50 (77)</td>
<td>121 (77)</td>
<td>1.00</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
<td>.24</td>
</tr>
<tr>
<td>EF (%)</td>
<td>63 ± 16</td>
<td>63 ± 17</td>
<td>.84</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>144 ± 30</td>
<td>149 ± 33</td>
<td>.40</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>67 ± 13</td>
<td>67 ± 10</td>
<td>.87</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td>30 (46)</td>
<td>65 (41)</td>
<td>.55</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>37 (57)</td>
<td>90 (57)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>43 (66)</td>
<td>97 (61)</td>
<td>.54</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>15 (21)</td>
<td>46 (29)</td>
<td>.41</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>23 (35)</td>
<td>56 (35)</td>
<td>1.00</td>
</tr>
<tr>
<td>PVD, n (%)</td>
<td>12 (18)</td>
<td>31 (20)</td>
<td>1.00</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>6 (9)</td>
<td>19 (12)</td>
<td>.64</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>30 (46)</td>
<td>64 (40)</td>
<td>.46</td>
</tr>
<tr>
<td>Redo-CABG, n (%)</td>
<td>12 (18)</td>
<td>19 (12)</td>
<td>.21</td>
</tr>
<tr>
<td>CABG to angio Time (mo)</td>
<td>118 ± 78</td>
<td>126 ± 82</td>
<td>.19</td>
</tr>
<tr>
<td>Clinical presentation, n (%)</td>
<td></td>
<td></td>
<td>.30</td>
</tr>
<tr>
<td>Stable angina</td>
<td>53 (81)</td>
<td>117 (74)</td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>12 (18)</td>
<td>41 (26)</td>
<td></td>
</tr>
</tbody>
</table>

Di Serafino L et al. Am Heart J 2013
## Procedural characteristics

<table>
<thead>
<tr>
<th></th>
<th>FFR guided</th>
<th>Angio guided</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI performed, n (%)</td>
<td>23 (35)</td>
<td>90 (57)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>PCI on arterial grafts, n (%)</td>
<td>16 (70)</td>
<td>12 (13)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>PCI-related myocardial territory, n (%)</td>
<td>14 (61)</td>
<td>19 (21)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>LAD</td>
<td>14 (61)</td>
<td>19 (21)</td>
<td></td>
</tr>
<tr>
<td>LCx</td>
<td>5 (22)</td>
<td>32 (36)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>4 (17)</td>
<td>39 (43)</td>
<td></td>
</tr>
<tr>
<td>Embolic protection device, n (%)</td>
<td>0 (0)</td>
<td>3 (3)</td>
<td>.26</td>
</tr>
<tr>
<td>Stent per patient, n (%)</td>
<td>0.3 ± 0.5</td>
<td>0.7 ± 0.8</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>DES, n (%)</td>
<td>9 (14)</td>
<td>21 (13)</td>
<td>.83</td>
</tr>
<tr>
<td>Stent diameter (mm)</td>
<td>3.0 ± 0.3</td>
<td>3.5 ± 0.6</td>
<td>.06</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>16.9 ± 5.2</td>
<td>21.1 ± 12.2</td>
<td>.12</td>
</tr>
<tr>
<td>PCI deferred, n (%)</td>
<td>42 (65)</td>
<td>68 (43)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Myocardial deferred territory, n (%)</td>
<td>10 (24)</td>
<td>22 (32)</td>
<td>.47</td>
</tr>
<tr>
<td>LAD</td>
<td>10 (24)</td>
<td>22 (32)</td>
<td></td>
</tr>
<tr>
<td>LCx</td>
<td>16 (38)</td>
<td>27 (40)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>16 (38)</td>
<td>19 (28)</td>
<td></td>
</tr>
<tr>
<td>Procedural time (min)</td>
<td>68 ± 26</td>
<td>62 ± 33</td>
<td>.23</td>
</tr>
<tr>
<td>X-ray time (min)</td>
<td>19 ± 14</td>
<td>17 ± 11</td>
<td>.37</td>
</tr>
<tr>
<td>Contrast medium (mL)</td>
<td>277 ± 110</td>
<td>294 ± 112</td>
<td>.44</td>
</tr>
<tr>
<td>Cost of procedure (€)</td>
<td>2240 ± 652</td>
<td>2416 ± 522</td>
<td>.03</td>
</tr>
<tr>
<td>Inhospital outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMI, n (%)</td>
<td>1 (1)</td>
<td>18 (11)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>TIMI major bleeds, n (%)</td>
<td>1 (1)</td>
<td>3 (1)</td>
<td>1.00</td>
</tr>
<tr>
<td>AKIN, n (%)</td>
<td>0 (0)</td>
<td>5 (3)</td>
<td>.32</td>
</tr>
</tbody>
</table>
Clinical outcome

MACCE-free Survival (%)

0 25 50 75 100

Months

0 12 24 36 48

65 150

FFR-guided

Angio-guided

Di Serafino L et al. Am Heart J 2013
## Clinical outcome

<table>
<thead>
<tr>
<th>Overall</th>
<th>FFR guided</th>
<th>Angio guided</th>
<th>Unadjusted HR (95% CI)</th>
<th>P</th>
<th>PS-adjusted HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n (%)</td>
<td>10 (15)</td>
<td>29 (19)</td>
<td>0.81 (0.39-1.66)</td>
<td>.566</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Death or nonfatal MI, n (%)</td>
<td>12 (18)</td>
<td>50 (33)</td>
<td>0.52 (0.28-0.97)</td>
<td>.041</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Nonfatal MI, n (%)</td>
<td>3 (5)</td>
<td>24 (16)</td>
<td>0.28 (0.08-0.93)</td>
<td>.037</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CVA, n (%)</td>
<td>0 (0)</td>
<td>5 (3)</td>
<td>0.03 (0.0-0.87)</td>
<td>.384</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>9 (14)</td>
<td>33 (22)</td>
<td>0.60 (0.29-1.25)</td>
<td>.17</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TVF, n (%)</td>
<td>10 (15)</td>
<td>41 (27)</td>
<td>0.52 (0.26-1.03)</td>
<td>.061</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MACCE, n (%)</td>
<td>18 (28)</td>
<td>77 (51)</td>
<td>0.46 (0.28-0.77)</td>
<td>.003</td>
<td>0.47 (0.30-0.75)</td>
<td>.001</td>
</tr>
<tr>
<td><strong>Arterial grafts</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TVF, n (%)</td>
<td>3 (11)</td>
<td>7 (30)</td>
<td>0.11 (0.01-0.90)</td>
<td>.04</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MACCE, n (%)</td>
<td>4 (15)</td>
<td>13 (56)</td>
<td>0.22 (0.07-0.66)</td>
<td>.008</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Venous grafts</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TVF, n (%)</td>
<td>7 (18)</td>
<td>34 (27)</td>
<td>0.68 (0.30-1.53)</td>
<td>.35</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MACCE, n (%)</td>
<td>14 (37)</td>
<td>64 (50)</td>
<td>0.67 (0.37-1.19)</td>
<td>.17</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
Summary

• FFR-guided PCI of intermediate stenosis in bypass graft is safe and results in a better clinical outcome as compared with an Angio-guided PCI.

• This clinical benefit was more pronounced in arterial grafts, whereas it was limited to a reduced incidence of PMI in SVGs.

Di Serafino L et al. Am Heart J 2013
Conclusion

• There is a role for FFR-guidance in patients undergoing CABG

  ➡️ as long as your surgeons believe in FFR

• FFR assessment in by-pass graft is reliable as long as you are aware of potential pitfalls
THANK YOU
DEFER: Clinical Outcome at 5 Years

Rate of Death/MI after 5 years

- DEFER
  - FFR ≥ 0.75: 3.3%
  - FFR < 0.75: 15.7%

- PERFORM
  - FFR ≥ 0.75: 7.9%

P = 0.002
P = 0.003
P = 0.21

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NHJ Pijls et al JACC 2007
FAME trial

ABSOLUTE DIFFERENCE IN MACE-FREE SURVIVAL

- FFR-guided
- Angio-guided

Survival Free from Major Adverse Cardiac Events

Days since Randomization

1 month 2.9%
6 months 4.9%
12 months 5.1%
24 months 4.7%

P Tonino et al NEJM 2009
Poor correlation between angiographic and functional stenosis severity in MVD

FFR > 0.80

65%  20%  4%

Stenosis classification by angiography
Methods 1

Primary endpoint

The rate of major adverse cardiac events, defined as all cause death, myocardial infarction and target vessel revascularization during 36-month follow-up

Toth et al. Circulation 2013
Methods 2

Inclusion criteria

- Stable angina / unstable angina
- Catheterization in our department between 2006 and 2010
- Indication for Coronary Artery Bypass Graft Surgery
- Having at least one intermediate stenosis (DS 30-70%)

Exclusion criteria

- STEMI / NSTEMI
- Concomitant valvular surgery
Methods 3

Patients were divided into

**Angio-guided group**

If CABG occurred **without prior FFR** assessment of any intermediate stenosis. Grafting was justified purely by the angiographic severity

**FFR-guided group**

If CABG occurred **with prior FFR** assessment of **at least one** intermediate stenosis. Grafting was done with FFR $\leq 0.80$ or deferred with FFR $> 0.80$
<table>
<thead>
<tr>
<th></th>
<th>Angio-guided n=429</th>
<th>FFR-guided n=198</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>70 (63-76)</td>
<td>65 (56-72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>72</td>
<td>82</td>
<td>0.010</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27 (24-30)</td>
<td>28 (25-30)</td>
<td>0.069</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>79</td>
<td>78</td>
<td>0.917</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>67</td>
<td>65</td>
<td>0.587</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>30</td>
<td>22</td>
<td>0.034</td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>14</td>
<td>20</td>
<td>0.081</td>
</tr>
<tr>
<td>Previous PCI, %</td>
<td>24</td>
<td>49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking habit, %</td>
<td>41</td>
<td>42</td>
<td>0.794</td>
</tr>
<tr>
<td>Family history, %</td>
<td>24</td>
<td>24</td>
<td>1.000</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>71 (60-80)</td>
<td>71 (61-79)</td>
<td>0.931</td>
</tr>
</tbody>
</table>
Sub-analysis

Analysed grafts were divided in two groups according to the guidance of revascularization:

**Angio-guided grafts**

Graft was placed on a vessel with intermediate stenosis, based on angiographic appearance

**FFR-guided grafts**

Graft was placed on a vessel with intermediate stenosis, based on proven functional significance (FFR ≤ 0.80)
Graft Patency After FFR-guided versus Angio-guided CABG: a randomized clinical trial (GRAFFITI trial)

www.clinicaltrial.gov NCT01810224

Principal investigators:
Emanuele Barbato
Bernard De Bruyne
Gabor Toth
Patient with
- Significant LAD / LM lesion AND
- At least one more lesion

~ 200 pts
- proved by FFR (<0.80) / Angio (>69%)
- angiographically intermediate (30-90%)

DS 30 - 90%

FFR measurement

FFR blinded HEART TEAM consultation
(Surgeons will be asked to identify by visual estimation the target vessels to be revascularized, number of anastomosis and grafts)

PATIENT 1:1 RANDOMIZATION

FFR-GUIDED GROUP
INFORM surgeons about FFR-values

ANGIO-GUIDED GROUP
Let surgeons BLINDED for FFR-values

GRAFT ONLY THE FUNCTIONALLY SIGNIFICANT LESIONS

GRAFT ALL THE ANGIOGRAPHICALLY SIGNIFICANT LESIONS

12 ± 2M FOLLOW-UP

GRAFT PATENCY CONTROLLED BY CCTA and/or CA
Endpoints

Primary: - Rate of **occluded grafts** at 12M FU

Secondary: - Graft **patency** at 12M FU (defined as average percent of patent graft per patient)
- Perioperative **myocardial infarction** and **periprocedural necrosis**
- Changes in Syntax Score classification regarding to Angio-guided vs FFR guided calculation
- Length of **hospitalization** after surgery
- **Cost of Care**: defined as costs of index hospitalization, re-hospitalization, repeat revascularization (redo-CABG or PCI)
- Changes in **surgical strategy** depending upon FFR results i.e. Open-chest vs. Minithoracotomy, On-pump vs. Off-pump, etc. (*in FFR-guided group only*)
- Changes in **functional state** (CCS classification)
- Rate of **Major Adverse Cardiovascular Events** (Death, Myocardial Infarction, Symptom-driven revascularisation)
Methods 1

Primary endpoint

The rate of major adverse cardiac and cerebrovascular events (MACCEs), defined as all cause death, non-fatal infarction, target vessel failure and cerebrovascular events.
Methods 2

Inclusion criteria

- Stable angina / unstable angina
- Catheterization in our department between 2000 and 2011
- Having at least one intermediate stenosis (40-70%) of an arterial or a venous bypass graft

Exclusion criteria

- STEMI / NSTEMI
- Presence of serial stenosis located in bypass graft or in both bypass graft and its subtended native vessel
- Presence of sequential anastomosis in the target bypass graft

Di Serafino L et al. Am Heart J 2013
Methods 3

Patients were divided into:

**Angio-guided group**

If PCI of an intermediate bypass graft stenosis was performed or deferred based on the angiographic appearance of the coronary lesion

**FFR-guided group**

If PCI of an intermediate bypass graft stenosis was performed in case of FFR ≤ 0.80 and deferred to medical therapy in case of FFR > 0.80
Patient with
- Significant LAD / LM lesion
  AND
- At least one more lesion

\(~200\) pts
- proved by FFR (<0.80) / Angio (>69%)
- angiographically intermediate (30-90%)

\[\text{DS 30 - 90%}\]

\[\text{FFR measurement}\]

\[\text{FFR blinded HEART TEAM consultation}\]
\(\text{(Surgeons will be asked to identify by visual estimation the target vessels to be revascularized, number of anastomosis and grafts)}\)

\[\text{PATIENT 1:1 RANDOMIZATION}\]

\[\text{FFR-GUIDED GROUP}\]
- INFORM surgeons about FFR-values
- GRAFT ONLY THE FUNCTIONALLY SIGNIFICANT LESIONS

\[\text{ANGIO-GUIDED GROUP}\]
- Let surgeons BLINDED for FFR-values
- GRAFT ALL THE ANGIOGRAPHICALLY SIGNIFICANT LESIONS

\[\text{12} \pm 2\text{M FOLLOW-UP}\]

\[\text{GRAFT PATENCY CONTROLLED BY CCTA and/or CA}\]