Dolore Toracico: Il Corretto Approccio ed il Valore Incrementale de “Multimodality Imaging” nei Pazienti con Rischio di Malattia Basso-intermedio

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Anatomy and physiology in ischaemic heart disease: a second honeymoon?

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Anatomy and physiology in ischaemic heart disease: a second honeymoon?

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THE PHASE OF DIVORCE: anatomy or physiology?

However, this marriage was troubled by reports suggesting that more than two-thirds of acute myocardial infarctions may have non obstructive coronary artery stenosis.

**Shaw L et al, CIRCULATION 2008**

- Stenoses > 70%
  - Moderate Ischemia: 40%
  - Mild Ischemia: 32%
  - No ischemia: 28%

**Tonino PA et al, NEJM 2009**

- Stenoses > 70%
  - Ischemia: 20%
  - No ischemia: 80%

- Stenoses < 50%
  - Ischemia: 17%
  - No ischemia: 83%
The "ischemic approach" alone is not enough efficient as gatekeeper for ICA

«Which alternative to functional strategy in patients with suspected coronary artery disease?»
THE PHASE OF DIVORCE: role of CCT

Neglia D et al, Circulation CI 2015 (EVINCI Trial)

CCT showed the highest accuracy in low to intermediate risk patients (prevalence of CAD 29%) as compared to other functional imaging modalities.

Douglas P et al, NEJM 2015 (PROMISE Trial)

In symptomatic intermediate risk patients (prevalence 53%) patients with suspected CAD who required non invasive testing, an initial strategy of CTA showed similar clinical outcome, QOL and cost as compared to functional testing.
How to improve the detection of coronary artery disease functionally significant with new emerging techniques?

1. Stress Cardiac Magnetic Resonance (CMR)
2. Fractional Flow Reserve CT (FFRct)
2. Stress CT perfusion (CTP)
1. Why do we need CMR in suspected CAD?

- **LV DILATATION AND LOW EF**
- **PERFUSION DEFECT**
- **WALL MOTION ABNORMALITIES**

**Table A2. Noninvasive Risk Stratification**

<table>
<thead>
<tr>
<th>High-risk (&gt;3% annual mortality rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Severe resting left ventricular dysfunction (LVEF &lt; 35%)</td>
</tr>
<tr>
<td>2. High risk treadmill score (score ≤ -11)</td>
</tr>
<tr>
<td>3. Severe exercise left ventricular dysfunction (exercise LVEF &lt; 35%)</td>
</tr>
<tr>
<td>4. Stress-induced large perfusion defect (particularly if anterior)</td>
</tr>
<tr>
<td>5. Stress-induced multiple perfusion defects of moderate size</td>
</tr>
<tr>
<td>6. Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
</tr>
<tr>
<td>7. Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
</tr>
<tr>
<td>8. Echocardiographic wall motion abnormality (involving &gt;2 segments) developing at low dose of dobutamine (≤ 10 mg/kg/min) or at a low heart rate (&lt;120 beats/min)</td>
</tr>
<tr>
<td>9. Stress echocardiographic evidence of extensive ischemia</td>
</tr>
</tbody>
</table>
1. Why do we need a functional test in suspected CAD?

2. Which is the diagnostic accuracy of stress CMR in suspected CAD?

Mean myocardial perfusion reserve (MPR) in stenotic (70%) territories. The best cutoff values for the detection of coronary artery disease (CAD) (MPR-CMR 1.45 and MPR-PET 1.44) are shown. CMR: cardiac magnetic resonance; PET: positron emission tomography.
The findings of CE-MARC support the wider adoption of CMR for the diagnosis and management of stable coronary heart disease patients, in view of the growing concern of the cancer risk associated with the medical source ionising radiation.

Greenwood JP Lancet 2012
THE PHASE OF DIVORCE: role of CMR

1. Why do we need a functional test in suspected CAD?
2. Which is the diagnostic accuracy of stress CMR in suspected CAD?
3. Which is the best protocol for stress CMR?
4. Which is the diagnostic accuracy of stress CMR versus other imaging modality?
5. Which is the prognostic stratification of stress CMR?

Adjusted survival curves without all cardiac events (left panel) and hard cardiac events (right panel) in patients without perfusion defect or AWM under stress (Group 1), in patients with perfusion defect without AWM under stress (Group 2) and in patients with perfusion defect plus AWM under stress (Group 3). AWM: abnormal wall motion

Pontone G, Eur Radiol 2015
ViosWorks

3D cardiac anatomy, function, and flow in 1 free-breathing, 8 min scan

42cm FOV
256 x 192
7:55 min

ViosWorks not commercially available
Expected availability 2016
How to improve the detection of coronary artery disease functionally significant with new emerging techniques?

1. Stress Cardiac Magnetic Resonance (CMR)
2. Fractional Flow Reserve CT (FFRct)
3. Stress CT perfusion (CTP)
THE PHASE OF DIVORCE: role of FFRct
The fractional flow reserve CCT derived (FFRct) is accurate even in challenging setting such as calcified calcified lesion. When compared to alternative strategy such as TAF, the FFRct has showed higher sensitivity and specificity.
THE PHASE OF DIVORCE: role of FFRct

HOW TO INCREASE THE COST EFFECTIVENESS OF THE GATEKEEPER TO ICA?

Prospective Longitudinal Trial of FFR<sub>CT</sub>: Outcome and Resource Impacts study

- THE PLATFORM trial -

Rationale and design of the Prospective Longitudinal Trial of FFR<sub>CT</sub>: Outcome and Resource Impacts study

Gianluca Pontone, MD, PhD, a Manesh R. Patel, MD, b Mark A. Hlatky, MD, c Karen Chiswell, PhD, b Daniele Andreini, MD, PhD, a Bjarne Linde Norgaard, MD, PhD, d Robert A. Byrne, MB, BCh, PhD, e Nick Curzen, BM, PhD, f Ian Purcell, MD, g Matthias Gutberlet, MD, PhD, b Gilles Rioufol, MD, PhD, i Ulrich Hink, MD, j Herwig W. Schuchlenz, MD, PhD, k Gudrun Feuchtner, MD, l Martine Gilard, MD, m Bernard de Bruyne, MD, PhD, n Campbell Rogers, MD, o and Pamela S. Douglas, MD b Milan, Italy; Durham, NC; Stanford, Redwood City, CA; Munich, Leipzig, Mainz, Germany; Southampton, Newcastle, United Kingdom; Lyon, Brest, France; Graz, Innsbruck, Austria; and Aalst, Belgium

(Am Heart J 2015;0:1-9.e44.)
THE PHASE OF DIVORCE: role of FFRct

HOW TO INCREASE THE COST EFFECTIVENESS OF THE GATEKEEPER TO ICA?

Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFRct: outcome and resource impacts study

Pamela S. Douglas¹, Gianluca Pontone², Mark A. Hlatky³, Manesh R. Patel¹, Bjarne L. Norgaard⁴, Robert A. Byrne⁵, Nick Curzen⁶, Ian Purcell⁷, Matthias Gutberlet⁸, Gilles Rioufol⁹, Ulrich Hink¹⁰, Herwig Walter Schuchlenz¹¹, Gudrun Feuchtnner¹², Martine Gilard¹³, Daniele Andreini¹², Jesper M. Jensen⁴, Martin Hadamitzky⁵, Karen Chiswell¹, Derek Cyr¹, Alan Wilk¹⁴, Furong Wang¹⁴, Campbell Rogers¹⁴, and Bernard De Bruyne¹⁵, On Behalf of the PLATFORM Investigators¹

- 61% patients in FFRct group: ICA cancelled
- Rate of ICA without obstructive CAD
  - By QCA: 73.3% usual care; 12.4% FFRct
  - By site-read angiographic
  - data: 56.7% usual care; 9.3% FFRct
THE PHASE OF DIVORCE: role of FFRct

- HOW TO INCREASE THE COST EFFECTIVENESS OF THE GATEKEEPER TO ICA?

Quality of Life and Economic Outcomes of Assessing Fractional Flow Reserve With Computed Tomography Angiography

The PLATFORM Study

Mark A. Hlatky, MD,* Bernard De Bruyne, MD, PhD,† Gianluca Pontone, MD, PhD,† Manesh R. Patel, MD,§
Bjame L. Norgaard, MD,‖ Robert A. Byrne, MB BCh, PhD,¶ Nick Curzen, BM (Hons), PhD,‖ Ian Purcell, MD,**
Matthias Gutberlet, MD,‖ Gilles Rioufol, MD,‡‡ Ulrich Hink, MD,§§ Herwig Walter Schuchlenz, MD,¶¶
Gudrun Feuchtnar, MD,¶¶ Martine Gilard, MD,### Daniele Andreini, MD,‡‡ Jesper M. Jensen, MD,¶¶
Martin Hadamitzky, MD,¶ Alan Wilk, BS,** Furong Wang, MD,*** Campbell Rogers, MD,*** Pamela S. Douglas, MD,§
for the PLATFORM Investigators
In conclusion, when used as an alternative diagnostic strategy to guide care in patients with planned invasive catheterization, CTA plus selective FFRCT was associated with a significantly lower rate of angiography showing no obstructive CAD, low rates of clinical outcomes, similar QOL, and significant cost savings. When used in those with planned noninvasive testing, clinical events were rare, and there were few differences in resource use, or QOL, although the small sample size in this group precludes firm conclusions.
Representative example of lesion with non-ischaemic RCA obstructive stenosis. A) Multiplanar reformat of CT demonstrating obstructive stenosis (white arrow) with no APCs (PR [−], LAP [−], SC [−]) in the proximal portion of RCA. B) Invasive coronary angiogram demonstrates obstructive stenosis (white arrow) and FFR value of 0.92 (red arrow), indicating vessel no-ischaemia. C) FFRCT value of 0.89 (red arrow) indicating vessel no-ischaemia.

Representative example of a lesion with ischaemic LAD obstructive stenosis. A) Multiplanar reformat of CT demonstrating obstructive stenosis (white arrow) with APCs (PR [+], LAP [+], SC [+]) in the proximal portion of LAD. B) Invasive coronary angiogram demonstrates obstructive stenosis (white arrow) and FFR value of 0.75 (red arrow), indicating vessel ischaemia. C) FFRCT value of 0.72 (red arrow) indicating vessel ischaemia. LAD: left anterior descending artery.
THE PHASE OF DIVORCE: role of FFRct

- HOW TO PREDICT THE PLAQUE RUPTURE?

EMERALD study

Exploring the MEchanism of the Plaque Rupture in Acute Coronary Syndrome using Coronary CT Angiography and Computational Fluid Dynamics

2012-06 Acute MI

Patients with Acute Coronary Syndrome
From 11 International Cardiovascular Centers
(Korea, Japan, Belgium, Denmark, the Netherlands)

Patients who underwent Coronary CT angiography before ACS event (1 month – 2 year before the event) (N=128)

Validation with clinical data, cCTA and coronary angiography

Final Enrollment for cCTA and CFD analysis (N=71)

CASE
Culprit Lesion (N=75)

CONTROL
Non-Culprit Lesion (N=151)

Screening Failure (N=45)
- No adequate CT image: 26
- Nuclear diagnosis: 14
- No definite culprit lesion on Angiography: 3

Exclusion by core laboratory due to CT image quality (N=12)

cCTA analysis
adverse plaque characteristics
(Core Lab – SNU Bundang Hospital)

CFD analysis
Non-invasive hemodynamics
(Core Lab - HeartFlow Inc.)
THE PHASE OF DIVORCE: role of FFRct

EMERALD study
Exploring the MEchanism of the Plaque Rupture in Acute Coronary Syndrome using Coronary CT Angiography and Computational Fluid Dynamics

Integrated cCTA (iCT) risk score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>High %DS (≥45.0%)</td>
<td>1</td>
</tr>
<tr>
<td>Any of APC</td>
<td>1</td>
</tr>
<tr>
<td>High Delta FFR (&gt;0.06)</td>
<td>1</td>
</tr>
<tr>
<td>Low FFR_{CT} (&lt;0.80)</td>
<td>1</td>
</tr>
<tr>
<td>High APS (&gt;12.7K)</td>
<td>1</td>
</tr>
</tbody>
</table>

Overall P < 0.001

Proportion of Culprit lesion:

- 0: 16.7%
- 1: 15.9%
- 2: 21.2%
- 3: 34.6%
- 4: 46.4%
- 5: 84.6%

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How to improve the detection of coronary artery disease functionally significant with new emerging techniques?

1. Stress Cardiac Magnetic Resonance (CMR)
2. Fractional Flow Reserve CT (FFRct)
3. Stress CT perfusion (CTP)
Visual assessment: Areas of reduced perfusion appear hypoenhanced compared with the normal myocardium, which implies either myocardial ischemia or myocardial infarction.

Strengths: Fast analysis

Pitfalls: Normal left ventricular myocardial enhancement demonstrates substantially lower attenuation in the lateral wall when compared with the anterior, septal, and inferior walls in patients with normal coronary arteries. The lateral myocardial wall is located adjacent to the air within the lungs and is not subjected to the same beam-hardening effect.
Quantitative assessment: Myocardial Blood Flow (MBF): maximum TAC slope/maximum AIF (ml/100 ml/min)

Images in a 75-year-old woman with typical symptoms of chest pain. (a) Curved multiplanar reformat of the left anterior descending coronary artery shows a subtotal occlusion of the middle left anterior descending coronary artery (arrow). (b) Stress myocardial CT perfusion color-coded map in a four-chamber view, from dynamic CT acquisition with a DS CT scanner, shows a hypoperfused area at the level of the septum and the apex (*). Both myocardial areas look thinner compared with the other myocardial segments. (c) MR image acquired with delayed enhancement in a four-chamber view.
Figure 3. Studies using coronary computed tomography angiography (CCTA) and computed tomography perfusion (CTP) compared with conventional coronary angiography (CCA) and fractional flow reserve (FFR) as the reference standard.
THE PHASE OF DIVORCE: role of CTP

OPEN ISSUES AND POTENTIAL SOLUTIONS
① Beam hardening and Dual Energy CT
THE PHASE OF DIVORCE: role of CTP

OPEN ISSUES AND POTENTIAL SOLUTIONS

② Heart Rate related artefacts and New generation CT scanner

- AF patients
THE PHASE OF DIVORCE: role of CTP

OPEN ISSUES AND POTENTIAL SOLUTIONS

③ Effective Radiation Dose and New generation CT scanner

Hi Res Lowdose CCTA @ 80 kV

Acquisition
Axial
80 kV
400 mA
0.28 sec/rot
50 ml CM+ 50 ml Saline fl. 5.0
HD Std kernel + ASiR V 50%
2.3 mGy CTDvol
37.6 mGy-cm DLP
0.5 mSv
20 BMI
Phase 75%
49 BPM
Rationale and design of the PERFECTION (comparison between stress cardiac computed tomography PERfusion versus Fractional flow rEserve measured by Computed Tomography angiography In the evaluation of suspected cOroNary artery disease) prospective study

Gianluca Pontone a,*, Daniele Andreini a, b, Andrea I. Guaricci c, d, Marco Guglielmo a, Saima Mushtaq a, Andrea Baggio a, Virginia Beltrama a, Daniela Trabattoni a, Cristina Ferrari a, Giuseppe Calligaris a, Giovanni Teruzzi a, Franco Fabbiochci a, Alessandro Lualdi a, Piero Montorsi a, b, Antonio L. Bartorelli a, b, Mauro Pepi a

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c Institute of Cardiovascular Disease, Department of Emergency and Organ Transplantation, University Hospital “Policlinico Consorziale” of Bari, Bari, Italy
d Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy
THE PHASE OF DIVORCE: role of CTP

Patients with pretest likelihood of CAD ≥ 50% scheduled for clinically indicated invasive coronary angiography and no contraindications to cCTA or FFR<sub>CT</sub>

**COHORT 1**
STATIC STRESS CTP
(N: 150 patients)

**COHORT 2**
DYNAMIC STRESS CTP
(N: 150 patients)

FFR<sub>CT</sub> – Visual CTP evaluation – Quantitative CTP (TPR & MBF)

ICA + Invasive FFR

**Figure 1. PERFECION study workflow.** CTP: computed tomography perfusion; FFR: fractional flow reserve; FFR<sub>CT</sub>: fractional flow reserve measured by computed tomography angiography; ICA: invasive coronary angiography; MBF: myocardial blood flow, TPR: transmural perfusion ratio.
THE PHASE OF DIVORCE: role of CTP

PATIENT PREPARATION
- Blood pressure
- ECG monitoring
- β-blockade i.v. administration
- Nitroprus i.v. administration

Rest CTA
- One beat whole heart coverage
- Tube voltage: 100 - 120 kVp
- Tube current: 500 mA

PAUSE

Adenosine i.v. injection
- (0.14 mg/Kg/min over 4 minutes)

Static Stress CTP
- 1 pass whole heart coverage
- Tube voltage: 100 - 120 kVp
- Tube current: 500 mA

Dynamic Stress CTP
- 15 passes sampling rate
- 10° free-breathing seq.
- Tube voltage: 100 - 120 kVp
- Tube current: 500 mA
Clinical case #1: A 83-year-old woman, known for recent onset of typical chest pain, performed SPECT, resulted positive for reversible perfusion deficit at mid-basal portion of postero-lateral wall.
Clinical case #1: A 83-year-old woman, known for recent onset of typical chest pain, performed SPECT, resulted positive for reversible perfusion deficit at mid-basal portion of postero-lateral wall.
Clinical case #1: A 83-year-old woman, known for recent onset of typical chest pain, performed SPECT, resulted positive for reversible perfusion deficit at mid-basal portion of postero-lateral wall.

FFR 0.67
Who is the winner?

“Diagnostic PERFORMANCE of stress echocardiography (Echo), stress single-photon-emission computed tomography (SPECT), positron emission tomography (PET), stress cardiac magnetic resonance (CMR), computed tomography coronary angiography (CTCA), stress perfusion computed tomography (CTP) and computed tomography fractional flow reserve (FFRCT) for the assessment of Coronary Artery Disease (CAD) versus invasive FFR (FFRi): a meta-analysis”
Summary of receiver operating characteristic curves for prediction of ischemia for a vessel (left panel) as compared to invasive FFR. The Q* statistic represents the point where sensitivity and specificity are equal.

AUC: area under the summary receiver operating characteristic curve; CMR cardiac magnetic resonance; CTCA computed tomography coronary angiography; CTP: stress myocardial computed tomography perfusion; Echo: stress echocardiography; FFR<sub>CT</sub>: Fractional Flow Reserve CT derived; PET positron emission tomography; SE: standard error; SPECT single-photon emission computed tomography.
A proposal of diagnostic algorithm to select patients with suspected CAD who could really receive benefits by ICA and consequential revascularization.

CAD: coronary artery disease; CMR: cardiac magnetic resonance; CTCA: computed tomography coronary angiography; FFR$_{CT}$: fractional flow reserve CTCA derived; ICA: invasive coronary angiography;
«Can we apply the same diagnostic work-up in revascularized patients?»
DIAGNOSTIC WORK-UP OF SYMPTOMATIC PATIENTS FOR CHEST PAIN WITH HISTORY OF REVASCULARIZATION

Ischemic Heart Disease

The STRATEGY Study (Stress Cardiac Magnetic Resonance Versus Computed Tomography Coronary Angiography for the Management of Symptomatic Revascularized Patients)

Resources and Outcomes Impact

Gianluca Pontone, MD, PhD, FESC, FSCCT; Daniele Andreini, MD, PhD, FESC, FSCCT; Andrea I. Guaricci, MD, FESC; Cristina Rota, MD; Marco Guglielmo, MD; Saima Mushtaq, MD; Andrea Baggiano, MD; Virginia Beltrama, MD; Laura Fusini, MSc; Anna Solbiati, MD; Chiara Segurini, MD; Edoardo Conte, MD; Paola Gripari, MD, PhD; Andrea Annoni, MD; Alberto Formenti, MD; Maria Petulla’, MD; Federico Lombardi, MD; Giuseppe Muscogiuri, MD; Antonio L. Bartorelli, MD, FESC, FACC; Mauro Pepi, MD, FESC

Pontone G et al, Circulation CI 2016
Which strategy (anatomical or functional) for revascularized patients?

Computed tomography coronary angiography versus stress cardiac magnetic resonance for the management of symptomatic revascularized patients: a cost effectiveness study (STRATEGY study)

![Graph showing comparison between CCT and CMR for downstream NI tests and rate of ICA.](Image)
DIAGNOSTIC WORK-UP OF SYMPTOMATIC PATIENTS FOR CHEST PAIN WITH HISTORY OF REVASCULARIZATION

Which strategy (anatomical or functional) for revasacularized patients?

Computed tomography coronary angiography versus Stress cardiac magnetic resonance for the management of symptomatic revascularized patients: a cost effectiveness study (STRATEGY study)

- Symptomatic stented pts
- CCT
- Stress-CMR

780±370 days

Downstream NI tests
Rate of ICA
Rate of PCI
Radiation exposure
Cumulative costs
MACES

Rate of revascularization

Radiation exposure

ED (mSv)

Pontone G et al, Circulation CI 2016
DIAGNOSTIC WORK-UP OF SYMPTOMATIC PATIENTS FOR CHEST PAIN WITH HISTORY OF REVASCULARIZATION

Which strategy (anatomical or functional) for revascularized patients?

Computed tomography coronary angiography versus Stress Cardiac Magnetic Resonance for the management of symptomatic revascularized patients: a cost effectiveness study (STRATEGY study)

In revascularized patients the functional strategy seems to be superior as compared to anatomical strategy in terms of cost-effectiveness.
Clinical case: CMR and planning of revascularization

✓ Male 66 yo with history of previous CABG (LIMA>LAD, SVG>LCX) symptomatic for angina
Clinical case: CMR and planning of revascularization

✓ Male 66 yo with history of previous CABG (LIMA>LAD, SVG>LCX) symptomatic for angina
A proposal of diagnostic algorithm to select patients with suspected CAD who could really receive benefits by ICA and consequential revascularization.

*CAD*: coronary artery disease; *CMR*: cardiac magnetic resonance; *CTCA*: computed tomography coronary angiography; *FFR*<sub>CT</sub>: fractional flow reserve *CTCA* derived; *ICA*: invasive coronary angiography;
NEW PERSPECTIVES

DECT vs. invasive FFR

FFR CT vs. Stress CMR/SPECT

The PERFECTION STUDY

FFR CT vs. Stress CTP

The PERFECTION STUDY

DETECT vs. invasive FFR
CONCLUSION


Anatomy and physiology in ischaemic heart disease: a second honeymoon?

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THANKS

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Hands on Cardiac Magnetic Resonance

January / December 2017

Course venue
Centro Cardiologico Monzino IRCCS, Milano

Hands on Cardiac CT

January / December 2017

Training course
Centro Cardiologico Monzino IRCCS, Milano

Centro Cardiologico Monzino

2017