There is still a place for thrombolysis in myocardial infarction - CON.

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COI: Dr Collet has nothing to declare with respect to this presentation (action-coeur.org).
The Goal

Coronary recanalisation

Myocardial reperfusion

Reduce myocardial necrosis

LV function preservation

Mortality reduction
The « lytic » era
Mortality reduction by treatment delay
(N=50,246)

65 (95% CI 38, 93) lives saved per 1000 treated patients vs 26 (14, 37)

The « percutaneous » era
Primary PCI is better than fibrinolysis

Pooled analysis of 23 randomized clinical trials
- N = 7739 thrombolytic-eligible patients with STEMI
- PPCI (n=3872) or thrombolytic therapy (n=3867)

Health-care-system delays* and long-term mortality

has the strongest association with long-term mortality among modifiable acute-phase covariates: HR of 1.22 (p<0.001) per 1 h increase in system delay.

JAMA 2010; 304: 763–71

*time from first medical contact to primary percutaneous coronary intervention
Summary
In observational studies, as D2B–D2N* times increase, the advantage of PPCI over fibrinolysis declines...

- N = 192,509 patients / 645 hospitals
- Odds of death for thrombolysis versus PPCI according to time

* D2B door-to-balloon / D2N door-to-needle

The sooner is the better

The pharmaco-invasive approach

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**Bleedings**

<table>
<thead>
<tr>
<th></th>
<th>Fibrinolysis (N=944)</th>
<th>PPCI (N=948)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH Any</td>
<td>9/939 (1.0)</td>
<td>2/946 (0.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>ICH After protocol amendment*</td>
<td>4/747 (0.5)</td>
<td>2/758 (0.3)</td>
<td>0.45</td>
</tr>
<tr>
<td>Nonintracranial bleeding Major</td>
<td>61/939 (6.5)</td>
<td>45/944 (4.8)</td>
<td>0.11</td>
</tr>
<tr>
<td>Nonintracranial bleeding Minor</td>
<td>205/939 (21.8)</td>
<td>191/944 (20.2)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

* On August 24, 2009, the study protocol was amended to reduce the dose of TNK by 50% in patients 75 years of age or older because of an excess of intracranial hemorrhage in this age group.

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P Sinnaeve AHA 2013
Why PCI is better?
Aim

- The aim of the exploratory ATLANTIC-H24 study was to examine more closely the effects of pre-versus in-hospital ticagrelor on reperfusion, platelet function and clinical endpoints during the first 24 h after primary PCI. The statistical analysis is exploratory.
Post-PCI coronary reperfusion

Pre-hospital ticagrelor

In-hospital ticagrelor

OR (95% CI):
1.132 (0.876–1.462)
p=0.3440

82.2%
80.4%
n=760
n=784

OR (95% CI):
1.225 (0.996–1.506)
p=0.0547

57.5%
52.5%
n=713
n=743

Median degree of resolution (%)

n=713
n=743

p=0.049a

TIMI flow grade 3 in MI culprit vessel

ST-segment elevation resolution ≥70%

Degree of ST-segment elevation resolution

n values are for subjects with PCI performed for the index event and available data on TIMI flow or ST-segment elevation.

aNon-parametric Wilcoxon test.
Randomized trials

- DO IT ALL DURING INDEX
  - ANGIO GUIDED
  - FFR GUIDED
- DO IT ALL STAGED
  - ANGIO GUIDED
  - FFR GUIDED
- IRA ONLY
  - BASED ON ISCHEMIC SYMPTOMS

PRAMI & CULPRIT

COMPARE ACUTE

DANAMI PRIMULTI

ESC Congress Paris 2019
Together with World Congress of Cardiology
COMPLETE Study Design N=(3900)

**STEMI Patients with successful culprit lesion PCI (primary, rescue or pharmaco-invasive)**
AND
≥70% stenosis in at least one additional non-culprit vessel that is at least 2.5 mm or ≥50% stenosis with FFR ≤0.80

RANDOMIZED within 72 h of index PCI

**COMPLETE REVASC**
Staged PCI of all suitable non-culprit lesions
N=1950

**CULPRIT LESION-ONLY REVASC**
No further revasc of non-culprit lesions (OMT Alone)
N=1950

ALL patients receive OMT (ASA, Ticagrelor, ACE-i/ARB, Statin, Beta Blocker)

Follow-up: Discharge, 6 Weeks, 6 Months, then annually (avg. duration = 4 yrs)

**Primary Outcome:** CV Death / MI
**Secondary Outcome:** CV Death/MI/Ischemia-driven revascularization
Figure 2 Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC (adapted from Wijns et al.).

*The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).
What is new in 2017 Guidelines on AMI-STEMI

2017 NEW / REVISED CONCEPTS

MINOCA AND QUALITY INDICATORS:
• New chapters dedicated to these topics.

STRATEGY SELECTION AND TIME DELAYS:
• Clear definition of first medical contact (FMC).
• Definition of “time 0” to choose reperfusion strategy (i.e. the strategy clock starts at the time of
  “STEMI diagnosis”).
• Selection of PCI over fibrinolysis: when anticipated delay from “STEMI diagnosis” to wire crossing is ≤120 min.
• Maximum delay time from “STEMI diagnosis” to bolus of fibrinolysis agent is set in 10 min.
• “Door-to-Balloon” term eliminated from guidelines.

TIME LIMITS FOR ROUTINE OPENING OF AN IRA:
• 0-12h (Class I); 12-48h (Class IIa); >48h (Class III).

ELECTROCARDIOGRAM AT PRESENTATION:
• Left and right bundle branch block considered equal for recommending urgent angiography if ischaemic
  symptoms.

TIME TO ANGIOGRAPHY AFTER FIBRINOLYSIS:
• Timeframe is set in 2-24h after successful fibrinolysis.

PATIENTS TAKING ANTICOAGULANTS:
• Acute and chronic management presented.
Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

Total ischaemic time

Patient delay

EMS delay

System delay

**Total ischaemic time**

**Patient delay**

**EMS delay**

**System delay**

FMC: EMS

<10’

STEMI diagnosis

<10’

FMC: Non-PCI centre

<10’

FMC: PCI centre

<10’

STEMI diagnosis

≤120 min

Primary PCI strategy

<90’

Reperfusion (Wire crossing)

>120 min

Fibrinolysis strategy

<10’

Reperfusion (Lytic bolus)

≤120 min

>120 min

<60’

Primary PCI strategy

<60’

Reperfusion (Wire crossing)
**Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>STEMI diagnosis</td>
<td>The time at which the ECG of a patient with ischaemic symptoms is interpreted as presenting ST-segment elevation or equivalent.</td>
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</table>

**Ambiguous terms are eliminated:**
- "Door-to-balloon"
- "Door to door"

**Total ischaemic time**

<table>
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<tr>
<th>Patient delay</th>
<th>EMS delay</th>
<th>System delay</th>
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- **STEMI diagnosis**
  - FMC: EMS <10’
  - FMC: Non-PCI centre <10’
  - FMC: PCI centre <10’

- **STEMI diagnosis**
  - Primary PCI strategy <60’
  - Reperfusion (Wire crossing)

www.escardio.org/guidelines

This Task Force recognizes the lack of contemporaneous data to set the limit to choose PCI over fibrinolysis. For simplicity, an absolute time from STEMI diagnosis to PCI-mediated reperfusion [i.e. wire crossing of the infarct-related artery (IRA)] rather than a relative PCI-related delay over fibrinolysis has been chosen. This limit is set to 120 min. Given the maximum limit of 10 min from STEMI diagnosis to bolus of fibrinolytics (see below), the 120 min absolute time would correspond to a PCI-related delay in the range of 110–120 min, being in the range of the times identified in old studies and registries as the limit delay to choose PCI.
Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

<table>
<thead>
<tr>
<th>Atypical ECG presentations</th>
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<tbody>
<tr>
<td>• Bundle branch block,</td>
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<tr>
<td>• Ventricular pacing,</td>
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<tr>
<td>• Hyper-acute T waves,</td>
</tr>
<tr>
<td>• Isolated depression in anterior leads,</td>
</tr>
<tr>
<td>• Universal ST depression with aVR elevation</td>
</tr>
</tbody>
</table>

Left and right bundle branch block are considered equal for recommending urgent angiography if ischaemic symptoms.

In the presence of symptoms, a primary PCI strategy (urgent angiography and PCI if indicated) should be followed.

Patient delay

System delay

Total ischaemic time

 STEMI diagnosis

≤120 min  Primary PCI strategy  <90'  Reperfusion (Wire crossing)

>120 min  Fibrinolysis strategy  <10'  Reperfusion (Lytic bolus)

Time to PCI?

Primary PCI strategy  <60'  Reperfusion (Wire crossing)
The MICU prospective
2 MICU = Mobile Intensive Care Unit

- Patient Diagnosis
- Prehospital Treatment
- Direct transfer
- Impact on clinical trials
Paris City Public STEMI Network

Pop = 2 168 000

Higher Density in the East Side ++

PCI 24/24H

Emergency Dept
2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC)

Endorsed by cardiac societies
Armenian Cardiologists Association, Austrian Society of Cardiology, Belgian Society of Cardiology, Belorussian Scientific Society of Cardiologists, Association of Cardiologists of Bosnia & Herzegovina, Bulgarian Society of Cardiology, Croatian Cardiac Society, Czech Society of Cardiology, Danish Society of Cardiology, Egyptian Society of Cardiology, Estonian Society of Cardiology, Finnish Cardiac Society, French Society of Cardiology, Georgian Society of Cardiology, German Cardiac Society, Hellenic Society of Cardiology, Hungarian Society of Cardiology, Italian Federation of Cardiology, Association of Cardiologists of Kazakhstan, Latvian Society of Cardiology, Lithuanian Society of Cardiology, Maltese Cardiac Society, Moroccan Society of Cardiology, Norwegian Society of Cardiology, Polish Cardiac Society, Portuguese Society of Cardiology, Romanian Society of Cardiology, Russian Society of Cardiology, San Marino Society of Cardiology, Cardiology Society of Serbia, Slovak Society of Cardiology, Spanish Society of Cardiology, Swedish Society of Cardiology, Swiss Society of Cardiology, Turkish Society of Cardiology

ESC Committee for Practice Guidelines (CPG) and National Cardiac Societies document reviewers: listed in the Appendix.

ESC entities having participated in the development of this document:
Associations: Acute Cardiovascular Care Association (ACCA), European Association of Preventive Cardiology (EAPC), European Association of Cardiovascular Imaging (EACVI), European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA).
Councils: Council on Cardiovascular Nursing and Allied Professions (CCNAP), Council for Cardiology Practice (CCP).
Working Groups: Cardiovascular Pharmacotherapy, Cardiovascular Surgery, Coronary Pathophysiology and Microcirculation, Myocardial and Pericardial Diseases, Thrombosis.
The golden two-hours time delay

The golden two-hours time delay

MICU-Arguments
« Early presenters » with pPCI in <60 min
Guidelines Adherence and outcome in STEMI

- N=22,160 (2003-2015) → 61% (13,569) of early presenters (<2 hours from SO-FMC)
- 35% of EP were eligible (n=7684) of whom 2839 had prehospital lytics (<15% of EP)

Guidelines Adherence and outcome in STEMI

Figure 2 Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC (adapted from Wijns et al.).

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Cash = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

* More than 4 hours → discuss
What do I see?
Palmarès 2018 et 2019

Institut de Cardiologie – Pitié-Salpêtrière
The Pitié-Salpêtrière network experience (2004-2007)

Symptom onset to FMC
- <2h: 51.5%
- <3h: 62.2%
- >4h: 28.4%

EKG- wire
- <90 min: 38.5%
- <120 min: 61.6%

Median PT was 110 minutes (57 min versus 324 min)
Transfer time (SO-angio) and mortality

After adjustment for confounding variables such as the severity of patients, the relationship between mortality and transfer time was no longer apparent.

Archives of Cardiovascular Disease (2012) 105, 639—648
The Pitié-Salpêtrière network experience (2007-2014)
Conclusions

- Better myocardial perfusion
- Time delay for oral drugs to be active
- Pharmaco-invasive is done in less than 10%
- Immediate appraisal of the coronary anatomy
- The best option for shock
Thank you
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Secondary Outcome: CV Death/MI/Ischemia-driven revascularization
Important timeline metrics in management of STEMI

Lancet 2013; 382: 624–32
One size does not fit all

The acceptable PCI vs thrombolysis related delay depends on patient age, infarct location, and symptom duration.

*Note that guidelines recommend a decision time of 120’ for all patients.