# *Nous devrions revasculariser complètement nos patients avec IAMEST*

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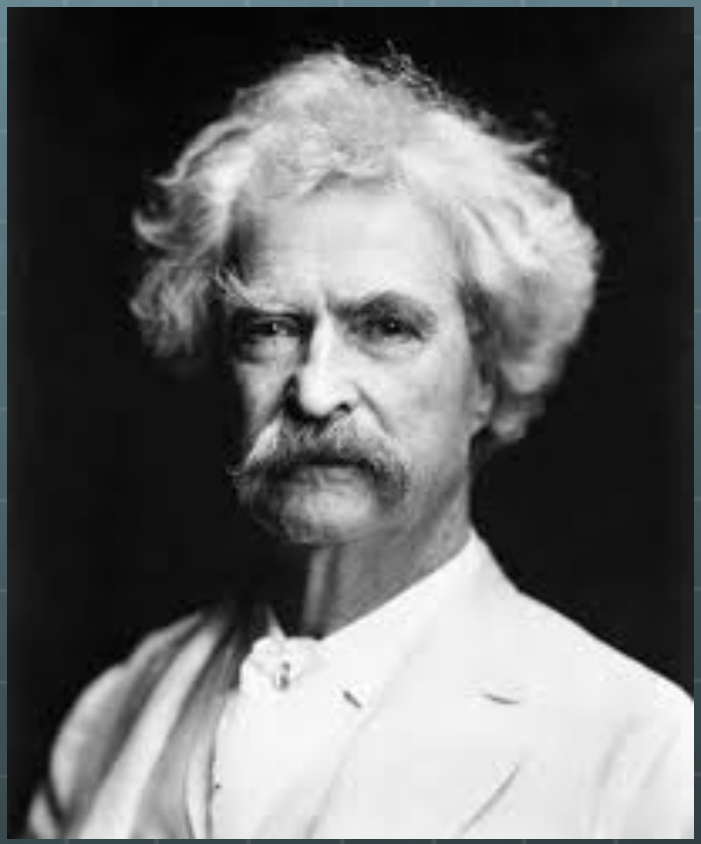
**Université de Sherbrooke**
**CIUSSS de l'Estrie - CHUS**

# Conflits d'intérêt potentiels

- Honoraires de présentation
  - Amgen
- Comités consultatifs
  - Bayer
  - BMS
  - Amgen
  - Sanofi
- Financement d'essais cliniques
  - Soundbite Medical Solutions
  - DalCor
- Actionnariat
  - Soundbite Medical Solutions

# Conflits d'intérêt potentiels



Mark Twain

"To a man with a hammer, everything looks like a nail."

# State the obvious !!!

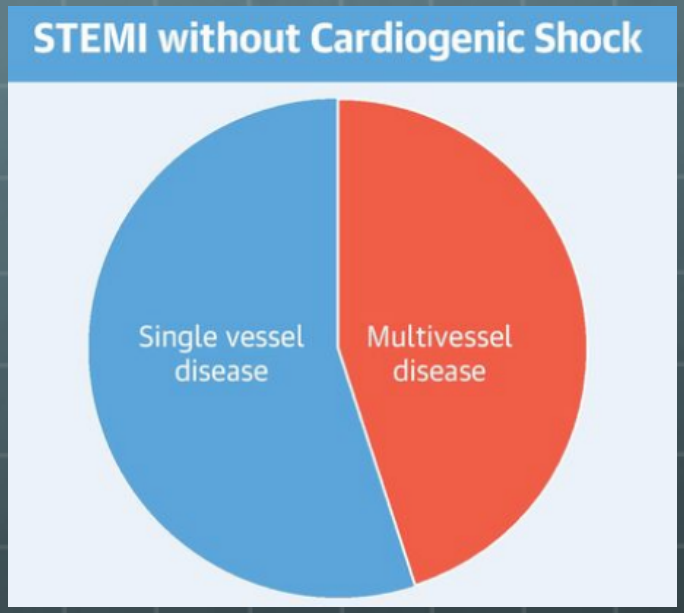
Less myocardial ischemia is good

REGION

Homicide victims rarely talk to police

# IAMEST et maladie pluritronculaire

**Population IAMEST**




*Lee, J.M et al. JACC 2018;71(8): 844-56*

**Lignes directrices ACC/AHA 2015**

**CLASS IIb (WEAK)** **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

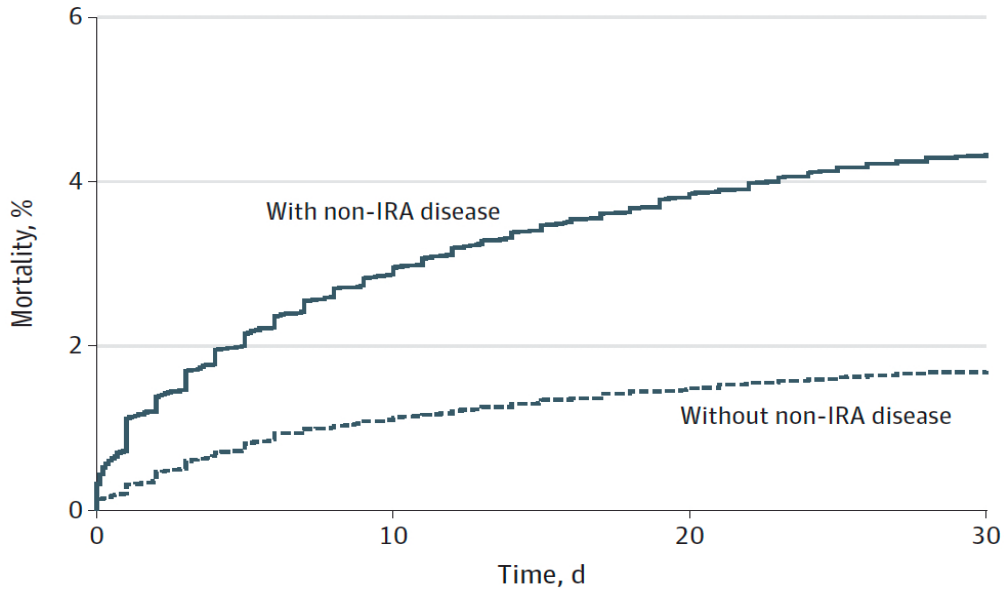
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

*Levine GN, et al. JACC 2016;67(10): 1235-50*

# *Pourquoi devrions-nous revasculariser complètement nos patients avec IAMEST ?*

# IAMEST et maladie pluritronculaire - pronostic

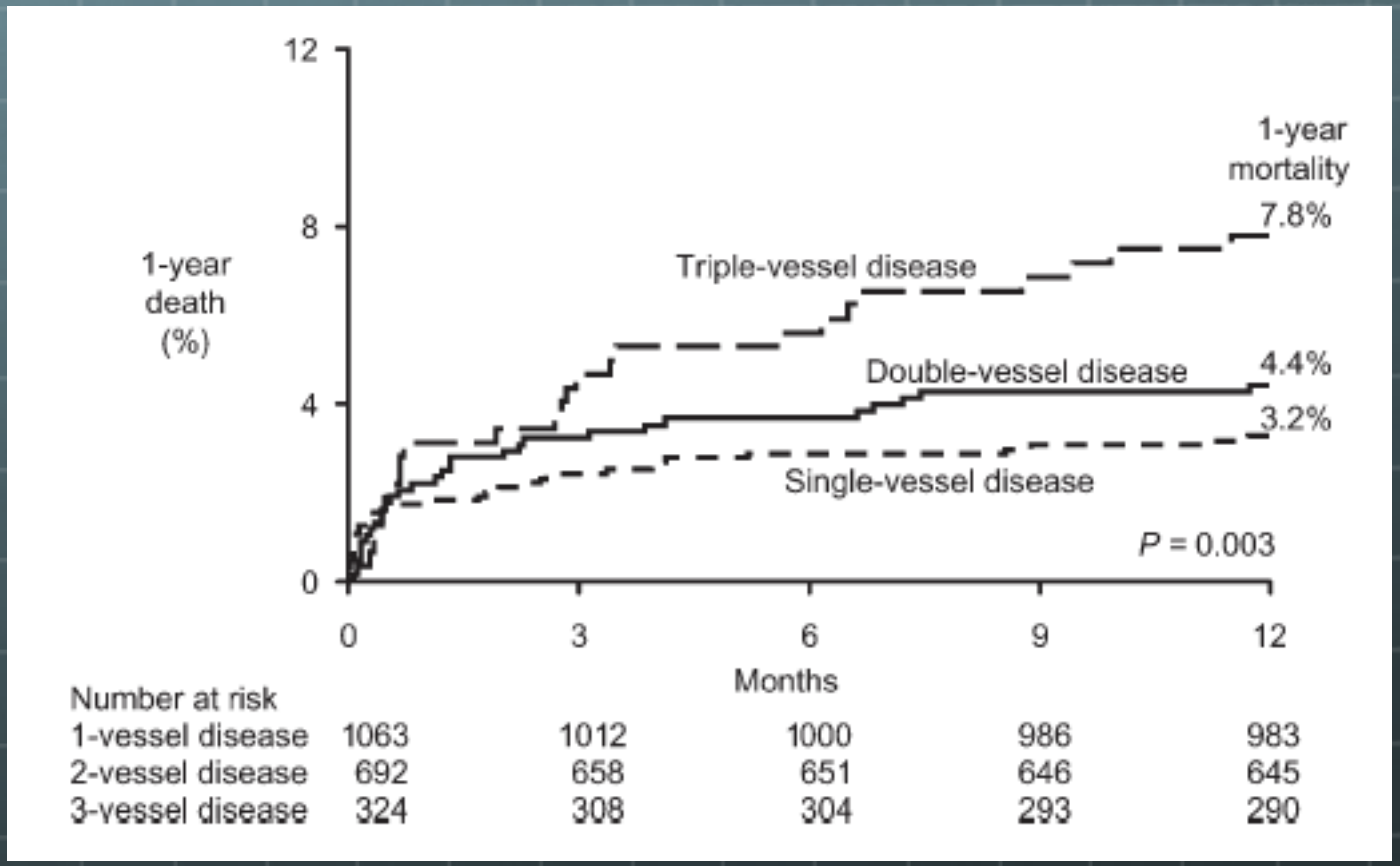
Figure 2. Kaplan-Meier Curve for 30-Day Mortality Between Patients With and Without Obstructive Non-Infarct-Related Artery (Non-IRA) Disease




| No. at risk | | | | |
|---|---|---|---|---|
| With non-IRA disease | 14 916 | 14 479 | 14 335 | 14 115 |
| Without non-IRA disease | 13 351 | 13 201 | 13 141 | 13 001 |

Park DW. Et al, JAMA. 2014;312(19):2019-2027

# IAMEST et maladie pluritronculaire - pronostic




*Sorajja P. et al, Eur H Journal (2007) 28, 1709–1716*

# *Premier constat*

La pluritroncularité en IAMEST est associé à un moins bon pronostic

# *Instabilité coronarienne diffuse*

MULTIPLE COMPLEX CORONARY PLAQUES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

JAMES A. GOLDSTEIN, M.D., DEMETRIS DEMETRIOU, M.D., CINDY L. GRINES, M.D., MARK PICA, B.S., MAZEN SHOUKFEH, M.D., AND WILLIAM W. O'NEILL, M.D.

- « … plaque instability is not merely a local vascular accident but probably reflects more generalized pathophysiologic processes with the potential to destabilize atherosclerotic plaques throughout the coronary tree. »

*Goldstein JA et al, N Engl J Med 2000;343:915-22*

# Instabilité coronarienne diffuse

**Multiple Coronary Lesion Instability in Patients With Acute Myocardial Infarction as Determined by Optical Coherence Tomography**

| | STEMI | MCAS stable | p |
|---|---|---|---|
| Sévérité angiographique | 72% | 73% | 0.6 |
| Fibrous cap thockness | 111 um | 181 um | 0.002 |
| TCFA | 38% | 6% | 0.03 |

Kubo T. et al, Am J Cardiol 2010;105:318 –22

# Instabilité coronarienne diffuse

- 20% des patients auront une récidive de SCA dans les 3 ans suivant l'évènement initial
- 55% des récidives se produiront sur des lésions >50% lors de la coronarographie initiale

**Table 3.** Independent Correlates of Major Adverse Cardiovascular Events Related to Nonculprit Lesions during Follow-up.*

| Correlates | Hazard Ratio (95% CI) | P Value |
|---|---|---|
| Predictors of events at individual lesion sites‡ | | |
| Plaque burden ≥70% | 5.03 (2.51–10.11) | <0.001 |
| Thin-cap fibroatheroma | 3.35 (1.77–6.36) | <0.001 |
| MLA ≤4.0 mm² | 3.21 (1.61–6.42) | 0.001 |

1. Lors d'un IAMEST, les lésions résiduelles ne sont pas des « innocent bystanders »
2. Les lésions sévères sont les plus susceptibles de causer une récidive de SCA

*Stone GW et al, N Engl J Med 2011;364:226-35*

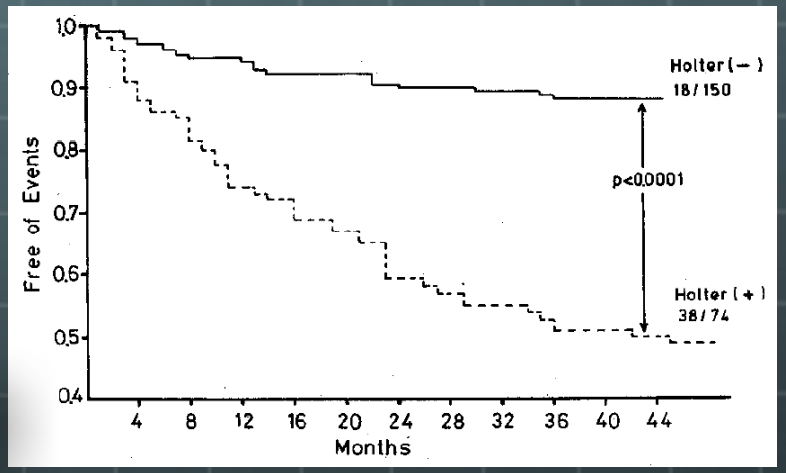
# *Deuxième constat*

Chez la population avec IAMEST, la maladie coronarienne résiduelle n'est pas une maladie stable

# L'ischémie myocardique résiduelle est néfaste

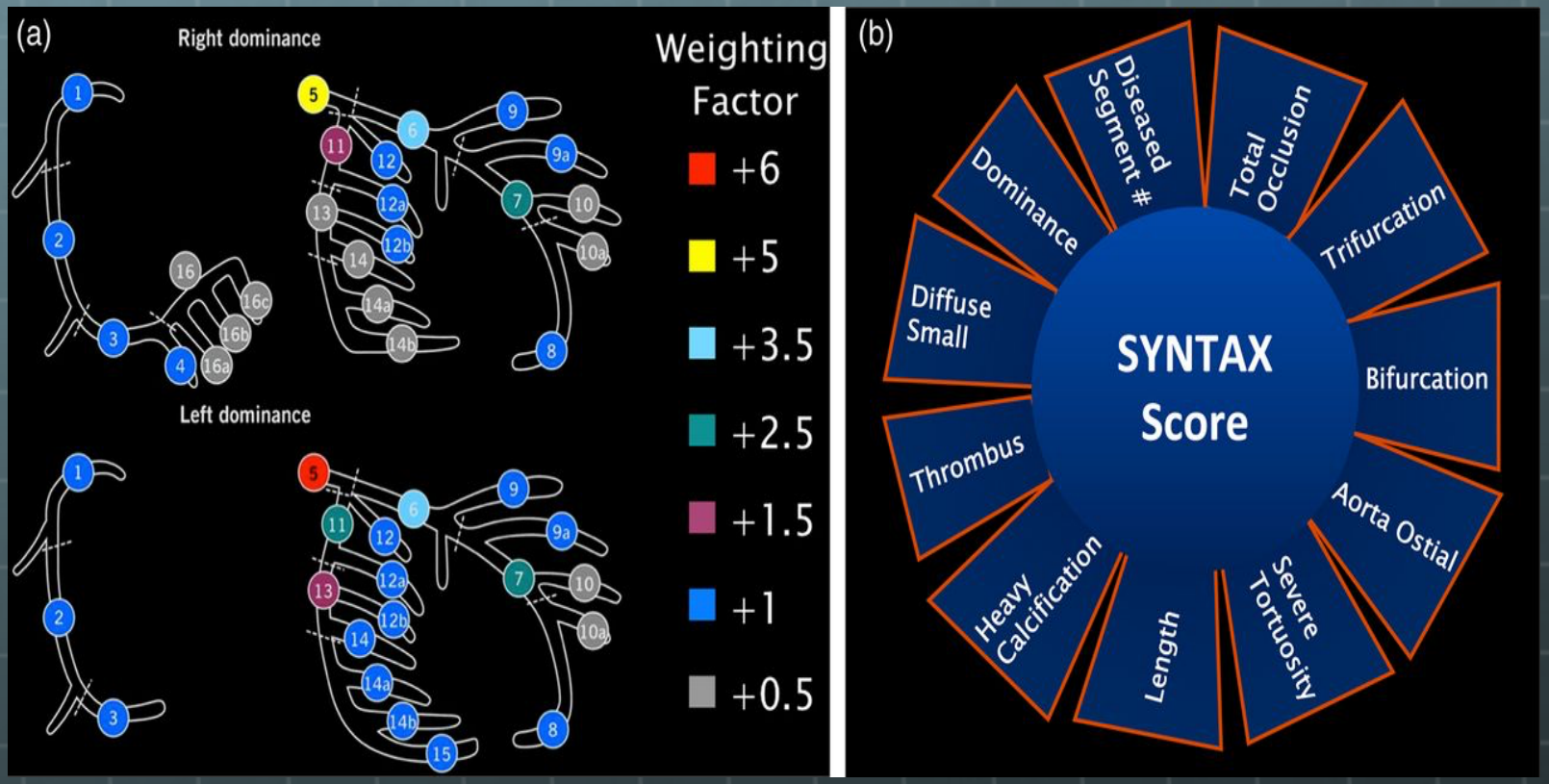
**TABLE I** Frequency of Cardiac Events in 224 Postinfarction Patients with Positive and Negative Holter Results

| | Pts (n) | Positive Holter Results (n = 74) | Negative Holter Results (n = 150) | p Value |
|---|---|---|---|---|
| Death | 8 | 4 (5.4%) | 4 (2.6%) | NS |
| Recurrent MI | 15 | 8 (10.8%) | 7 (4.7%) | NS |
| Unstable angina | 15 | 10 (13.5%) | 5 (3.3%) | <0.005 |
| Events | 38 | 22 (30%) | 16 (11%) | <0.0005 |




*Tzivoni D. at al, Am J Cardiol 1988 62;661-4*

# L'ischémie myocardique résiduelle est néfaste




Farooq V, *et al. Heart* 2014;100:276-287

# L'ischémie myocardique résiduelle est néfaste

| | RESIDUAL SYNTAX | | | | *P* |
|---|---|---|---|---|---|
| | <8 (n = 84) | | ≥8 (n = 36) | | |
| | NO. | % | NO. | % | |
| Repeated hospitalization | 0 | 0.0 | 12 | 33.3 | <0.001* |
| Angina | 0 | 0.0 | 20 | 55.6 | <0.001* |
| MACCE(1-year) | 9 | 10.7 | 11 | 30.5 | 0.020* |
| Death | 1 | 1.2 | 2 | 5.6 | 0.214 |
| Re-infarction | 4 | 4.8 | 3 | 8.3 | 0.427 |
| TVR | 1 | 1.2 | 4 | 11.1 | 0.028* |
| Non TVR | 3 | 3.6 | 5 | 13.8 | 0.025* |
| Repeat revascularization | 4 | 4.8 | 9 | 25 | 0.001* |
| Stroke | 0 | 0 | 0 | 0 | – |
| Death/MI/stroke | 5 | 6 | 5 | 13.9 | 0.016* |

Loufty L. et al, Clinical Medicine Insights: Cardiology 2016:10 29–35

# *Troisième constat*

Le pronostic des patients IAMEST avec maladie pluritronculaire est en lien avec la sévérité de l'ischémie résiduelle

# Donc…

1. La pluritroncularité en IAMEST est associé à un moins bon pronostic
2. Chez la population avec IAMEST, la maladie coronarienne résiduelle n'est pas une maladie stable
3. Le pronostic des patients IAMEST avec maladie pluritronculaire est lien avec la sévérité de l'ischémie résiduelle

Less myocardial ischemia is good

# State the obvious !!!

1. La pluritroncularité en IAMEST est associé à un moins bon pronostic
2. Chez la population avec IAMEST, la maladie coronarienne résiduelle n'est pas une maladie stable
3. Le pronostic des patients IAMEST avec maladie pluritronculaire est lien avec la sévérité de l'ischémie résiduelle

Less myocardial ischemia is good

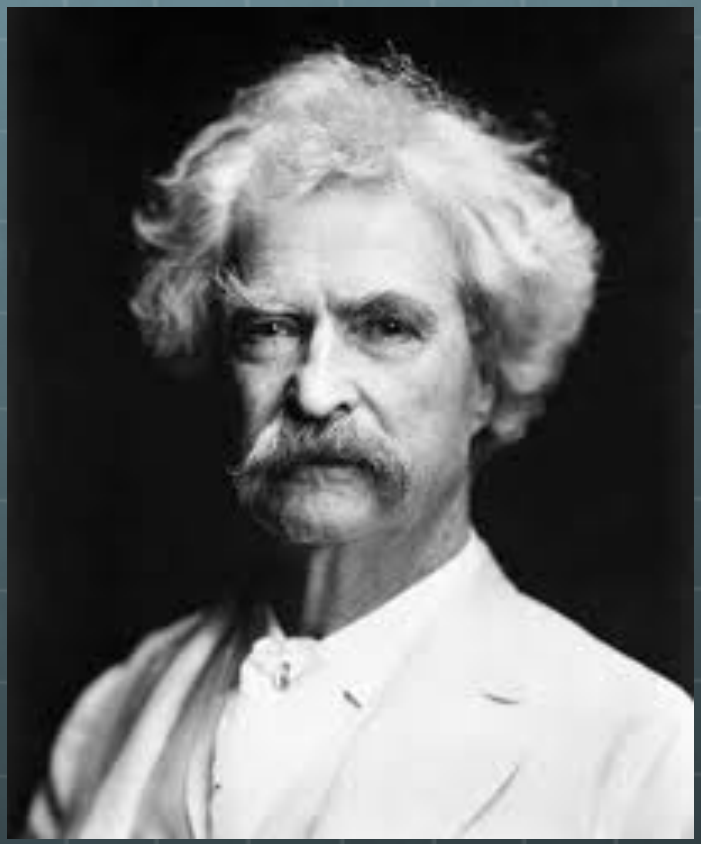
# État de l'évidence à ce jour

- 25 méta-analyses
  - 6 démontrent une augmentation de la mortalité après MV PCI
  - 10 démontrent une absence de différence de mortalité après MV PCI
  - 9 démontrent une diminution de la mortalité après MV PCI

mortality after MV PCI. Therefore, it is easy for an author to selectively cite a meta-analysis to support a conclusion or position on this topic for a publication,

Bates ER. et al, J Am Coll Cardiol 2016;68:1066–81

# État de l'évidence à ce jour



Mark Twain

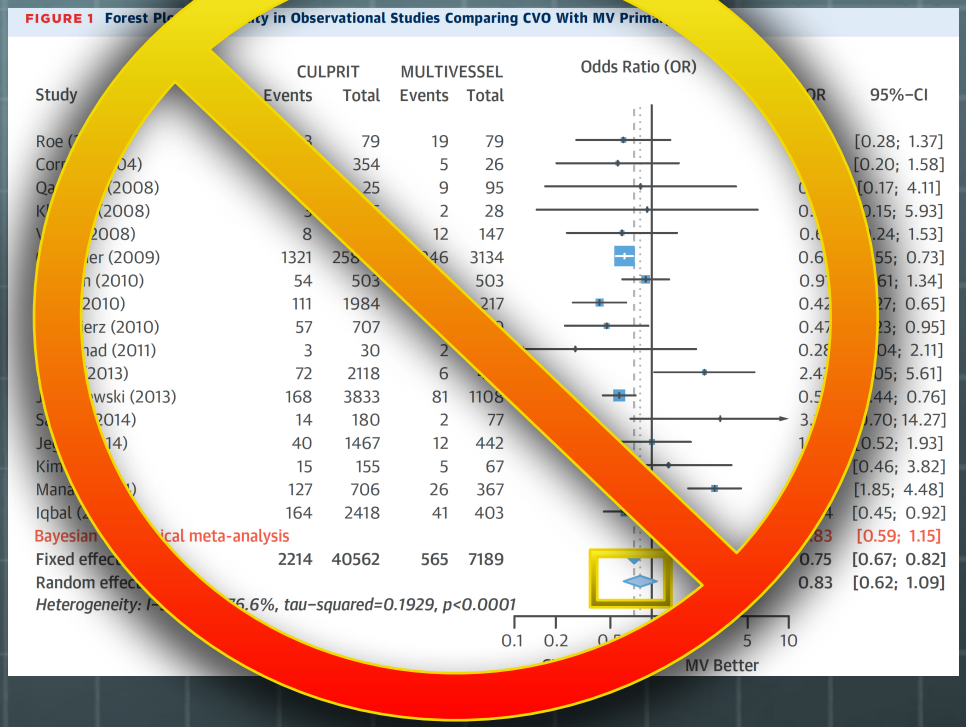
"Get your facts first, then you can distort them as you please."

« A caveat regarding the methodology of the study is that it is an observational study and is therefore subject to selection bias, whereby patients were chosen for 1 of the treatment options because of characteristics that would make that option more preferable and the other option less preferable. »

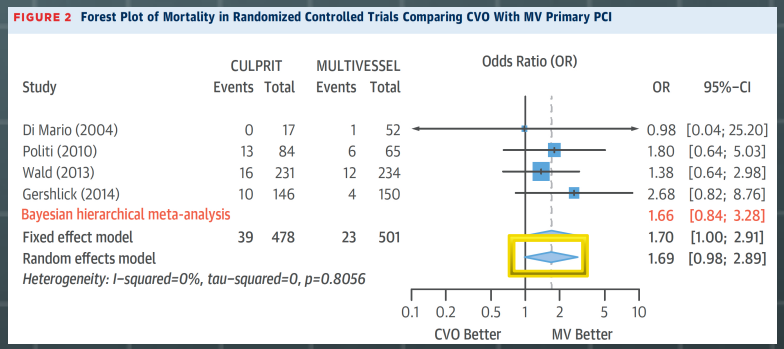
Hannan EL. et al, J Am Coll Cardiol Intv 2010;3:22–31

# État de l'évidence à ce jour

## Études observationnelles




## Études randomisées




**GIGO principle: Garbage In, Garbage Out.**

Bates ER. et al, J Am Coll Cardiol 2016;68:1066–81

# État de l'évidence à ce jour

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Random

David S. \
Alexanc
Lia
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Randomized Trial of Complete Versus Lesion-Only Revascularization in Patients Underg
Corona
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The CvLPR

Complete revascularisation versus treatment of the culprit lesion on
infarctio
an open-

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction

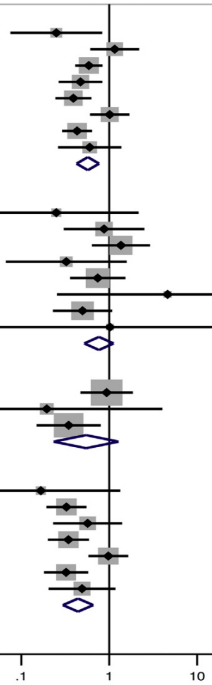
Pieter C. Smits, M.D., Ph.D., Mohamed Abdel-Wahab, M.D., Franz-Josef Neumann, M.D., Bianca M. Boxma-de Klerk, Ph.D., Ketil Lunde, M.D., Carl E. Schotborgh, M.D., Zsolt Piroth, M.D., David Horak, M.D., Adrian Wlodarczak, M.D., Paul J. Ong, M.D., Rainer Hambrecht, M.D., Oskar Angerås, M.D., Gert Richardt, M.D., Ph.D., and Elmir Omerovic, M.D., for the Compare-Acute Investigators*

# Études randomisées

**FIGURE 2** Pairwise Meta-Analysis

| Study | Year | RR (95% CI) | Events, Complete | Events, Culprit | % Weight |
|---|---|---|---|---|---|
| MACE | | | | | |
| Hamza et al | 2016 | 0.25 (0.08, 0.83) | 3/50 | 12/50 | 4.80 |
| PRAGUE 13 | 2015 | 1.15 (0.61, 2.19) | 17/106 | 15/108 | 11.24 |
| DANAMI-3-PRIMULTI | 2015 | 0.59 (0.41, 0.84) | 40/314 | 68/313 | 17.68 |
| CvLPRIT | 2015 | 0.47 (0.27, 0.84) | 15/150 | 31/146 | 12.57 |
| PRAMI | 2013 | 0.39 (0.24, 0.63) | 21/234 | 53/231 | 14.84 |
| Ghani et al | 2012 | 1.01 (0.60, 1.70) | 28/79 | 14/40 | 13.79 |
| Politi et al | 2010 | 0.43 (0.29, 0.64) | 28/130 | 42/84 | 16.82 |
| HELP-AMI | 2004 | 0.60 (0.26, 1.38) | 11/52 | 6/17 | 8.26 |
| Subtotal (I-squared = 56.6%, p = 0.024) | | 0.57 (0.42, 0.77) | 163/1115 | 241/989 | 100.00 |
| All-cause mortality | | | | | |
| Hamza et al | 2016 | 0.25 (0.03, 2.16) | 1/50 | 4/50 | 3.15 |
| PRAGUE 13 | 2015 | 0.87 (0.30, 2.51) | 6/106 | 7/108 | 12.93 |
| DANAMI-3-PRIMULTI | 2015 | 1.36 (0.63, 2.91) | 15/314 | 11/313 | 24.47 |
| CvLPRIT | 2015 | 0.32 (0.07, 1.58) | 2/150 | 6/146 | 5.81 |
| PRAMI | 2013 | 0.74 (0.36, 1.53) | 12/234 | 16/231 | 26.87 |
| Ghani et al | 2012 | 4.61 (0.25, 83.61) | 4/79 | 0/40 | 1.75 |
| Politi et al | 2010 | 0.50 (0.23, 1.08) | 10/130 | 13/84 | 23.55 |
| HELP-AMI | 2004 | 1.02 (0.04, 23.91) | 1/52 | 0/17 | 1.47 |
| Subtotal (I-squared = 1.6%, p = 0.417) | | 0.76 (0.52, 1.12) | 51/1115 | 57/989 | 100.00 |
| Re-infarction | | | | | |
| DANAMI-3-PRIMULTI | 2015 | 0.93 (0.47, 1.86) | 15/314 | 16/313 | 49.94 |
| CvLPRIT | 2015 | 0.19 (0.01, 4.02) | 0/150 | 2/146 | 7.12 |
| PRAMI | 2013 | 0.35 (0.15, 0.80) | 7/234 | 20/231 | 42.93 |
| Subtotal (I-squared = 47.5%, p = 0.149) | | 0.55 (0.23, 1.28) | 22/698 | 38/690 | 100.00 |
| Urgent revascularization | | | | | |
| Hamza et al | 2016 | 0.17 (0.02, 1.33) | 1/50 | 6/50 | 3.23 |
| DANAMI-3-PRIMULTI | 2015 | 0.33 (0.19, 0.55) | 17/314 | 52/313 | 18.75 |
| CvLPRIT | 2015 | 0.57 (0.23, 1.40) | 7/150 | 12/146 | 11.43 |
| PRAMI | 2013 | 0.34 (0.20, 0.59) | 16/234 | 46/231 | 18.42 |
| Ghani et al | 2012 | 0.98 (0.58, 1.65) | 27/79 | 14/40 | 18.83 |
| Politi et al | 2010 | 0.32 (0.18, 0.58) | 14/130 | 28/84 | 17.49 |
| HELP-AMI | 2004 | 0.49 (0.20, 1.18) | 9/52 | 6/17 | 11.85 |
| Subtotal (I-squared = 56.0%, p = 0.034) | | 0.44 (0.30, 0.66) | 91/1009 | 164/881 | 100.00 |

NOTE: Weights are from random effects analysis




← Better outcome with complete revascularization

Worse outcome with complete revascularization →

Elgendy IY. et al, J Am Coll Cardiol Intv 2017;10:315–24

# Études randomisées

**TABLE 2 Summary Estimates for the Outcomes in the Pairwise Meta-Analysis**

| Outcome | Incidence Complete/ Culprit-Only, %/% | Risk Ratio | 95% Confidence Interval | p Value |
|---|---|---|---|---|
| Major adverse cardiac events | 14.6/24.4 | 0.57 | 0.42–0.77 | <0.0001 |
| All-cause mortality | 4.6/5.8 | 0.76 | 0.52–1.12 | 0.17 |
| Spontaneous reinfarction | 3.1/5.5 | 0.54 | 0.23–1.27 | 0.16 |
| Urgent revascularization | 9.0/18.6 | 0.44 | 0.30–0.66 | <0.0001 |

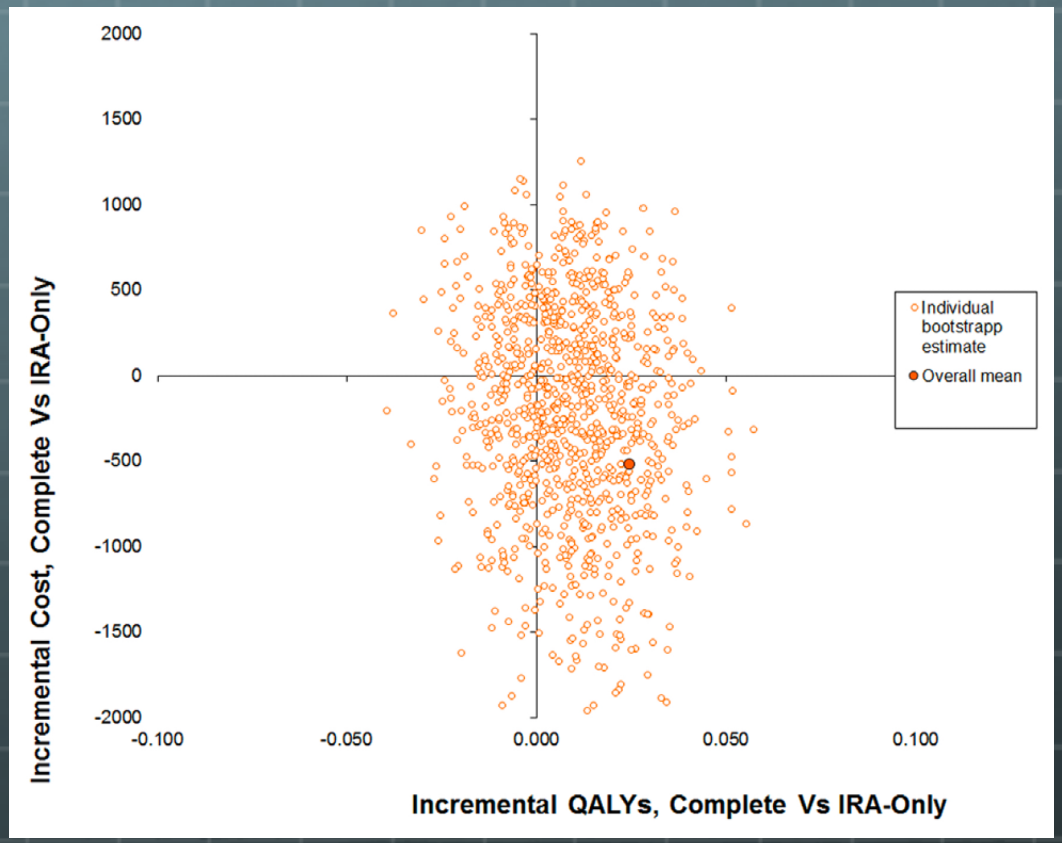
Elgendy IY. et al, J Am Coll Cardiol Intv 2017;10:315–24

# Dangers ??

| Outcome | Incidence Complete, %/culprit,% | RR | 95% CI | *P*-value |
|---|---|---|---|---|
| Major bleeding | 2.2/2.5 | 0.83 | 0.41–1.71 | 0.62 |
| Contrast-induced nephropathy | 1.6/1.7 | 0.94 | 0.42–2.12 | 0.89 |

Elgendy IY, et al. Catheterization and Cardiovascular Interventions 2016; 88:501–5

# Analyse coût-efficacité




Barton GR. Et al, Value in Health 20 (2017) 745-51

# Donc, chez les patients avec IAMEST:

1. La pluritroncularité est un prédicteur d'évolution néfaste
2. Le caractère instable des plaques coronariennes ne se limite pas à la lésion coupable, il est retrouvé dans l'ensemble de l'arbre coronarien
3. L'ischémie myocardique résiduelle est associé à une augmentation des évènements cardiovasculaires néfastes
4. L'intervention coronarienne percutanée des lésions ischémiques résiduelles visant une revascularisation complète  est associée à moins d'évènements cardiovasculaires néfastes et à une amélioration de la survie

We can no longer assume that secondary lesions in acute myocardial infarction are innocent until proven guilty

Dr Laura Mauri

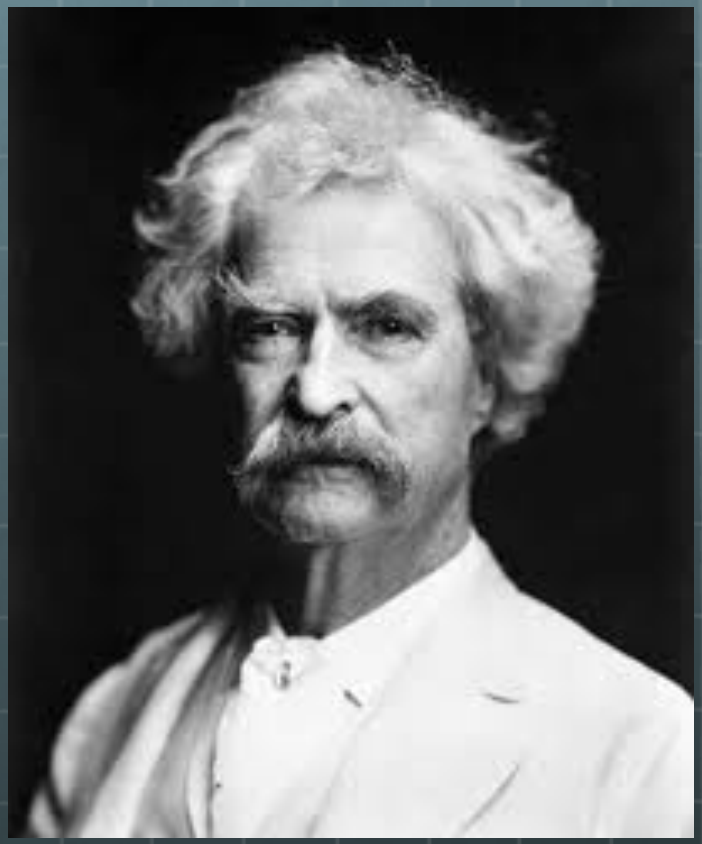
Mauri L, et al. NEJM 2013; 369:1166-7

# *Nous devrions donc revasculariser complètement nos patients avec IAMEST*

*Stating the obvious !!!*

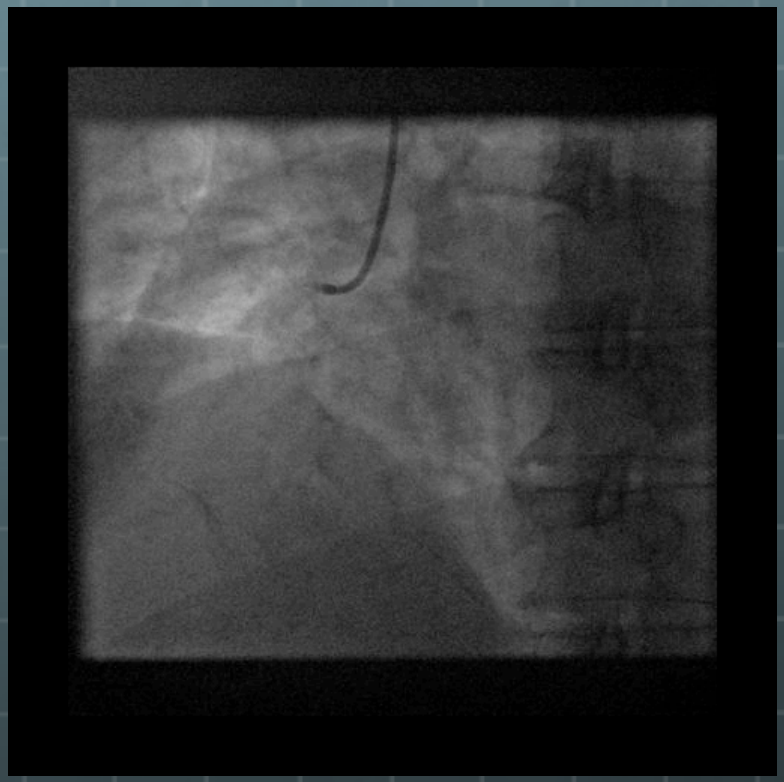
# *Nous devrions revasculariser complètement nos patients avec IAMEST*

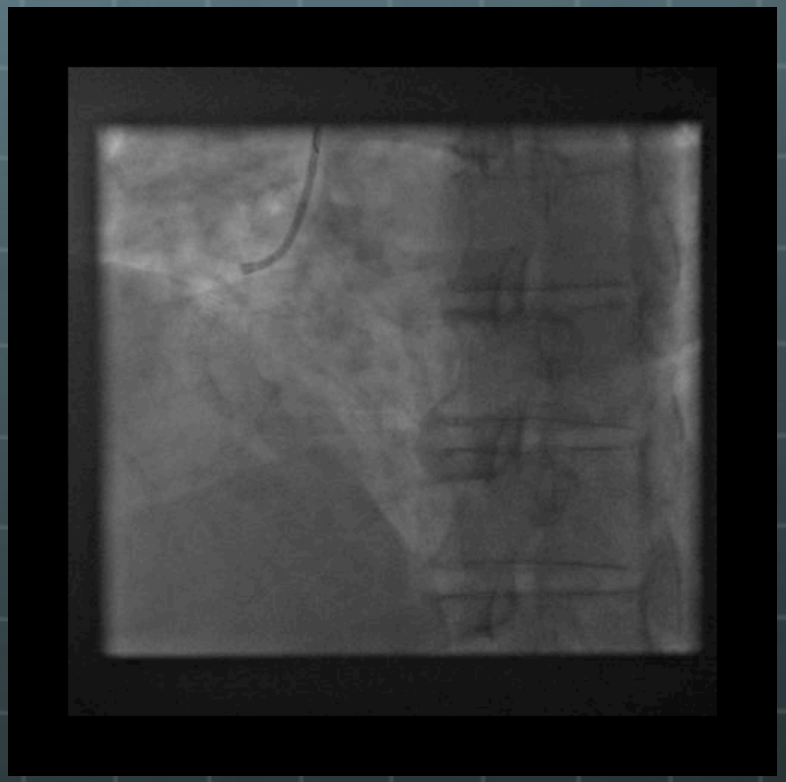
## Réplique



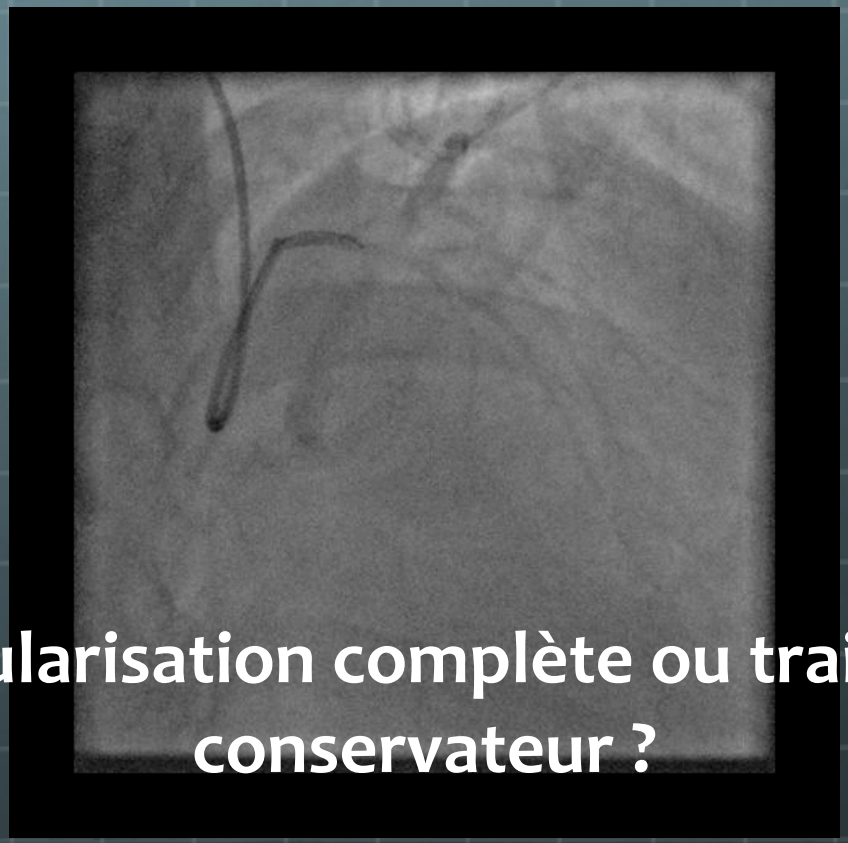
« Few things are harder to put up with than the annoyance of a good exemple. »

# Voici un bon exemple…



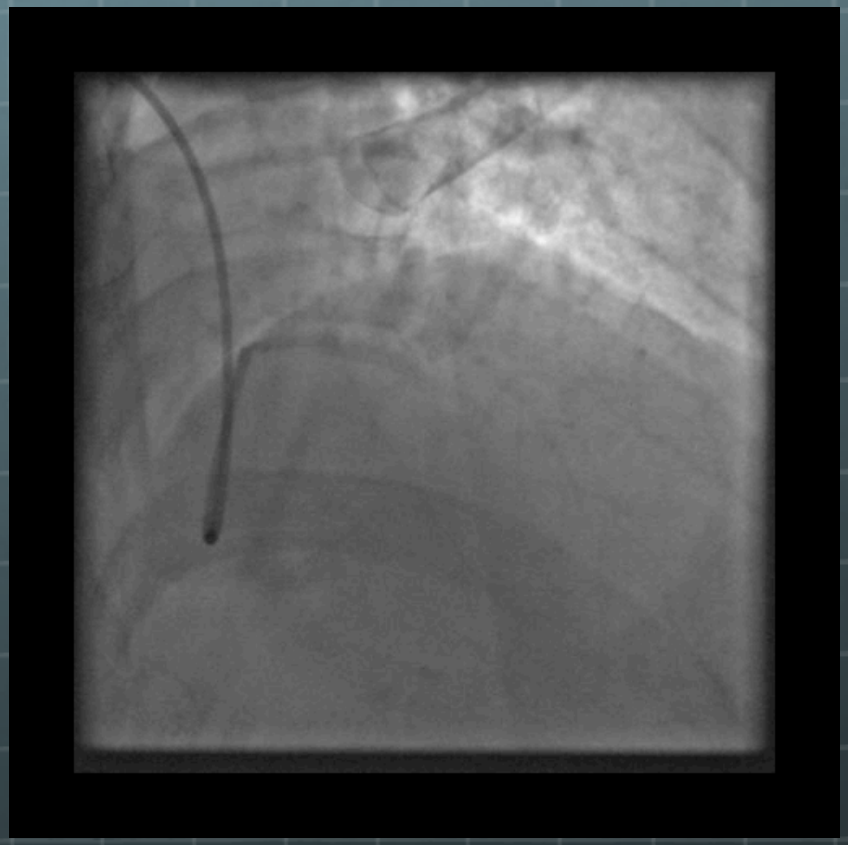


# *Voici un bon exemple…*

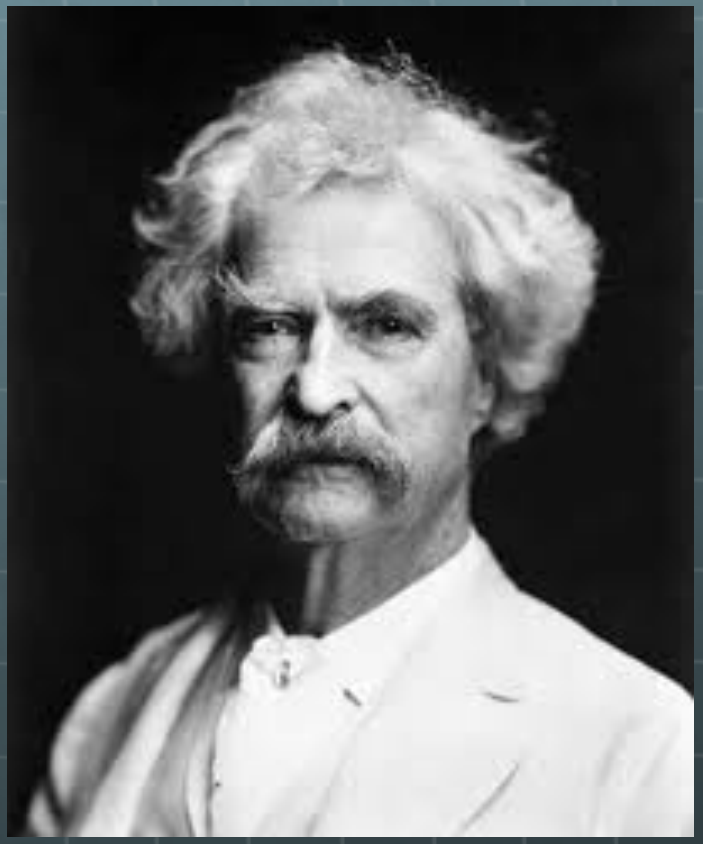


**Revascularisation complète ou traitement conservateur ?**

# Voici un bon exemple…



# *Dernière remarque pour Robert*



“Denial ain't just a river in Egypt.”

# Conclusion

Compared with CVO PCI, MV PCI, either at the time of primary PCI or as a staged procedure in selected patients who are hemodynamically stable, appears to be safe and may result in better outcomes. Whether MV primary PCI or staged PCI is superior remains to be demonstrated. Indications for noninfarct artery PCI should match elective PCI standards, with routine PCI of intermediate or complex stenoses at time of primary PCI discouraged. Until more definitive studies are available, physicians should integrate clinical status and comorbidities, lesion complexity, and clinical judgment to determine the optimal strategy and timing for PCI in patients with STEMI and MV CAD.

Bates ER. et al, J Am Coll Cardiol 2016;68:1066–81

# Conclusion

- Questions qui restent à répondre
  - ICP complémentaire pendant la procédure initiale ou dans un deuxième temps
  - Quelle est la place de la physiologie coronarienne pour orienter l'ICP complémentaire

Bates ER. et al, J Am Coll Cardiol 2016;68:1066–81

*Donc oui nous devrions revasculariser complètement nos patients avec IAMEST !*

*Merci*