BORDEAUX
15 NOVEMBRE 2019

# Détection de la coronaropathie asymptomatique chez les patients diabétiques
# *Où en est-on en 2019 ?*

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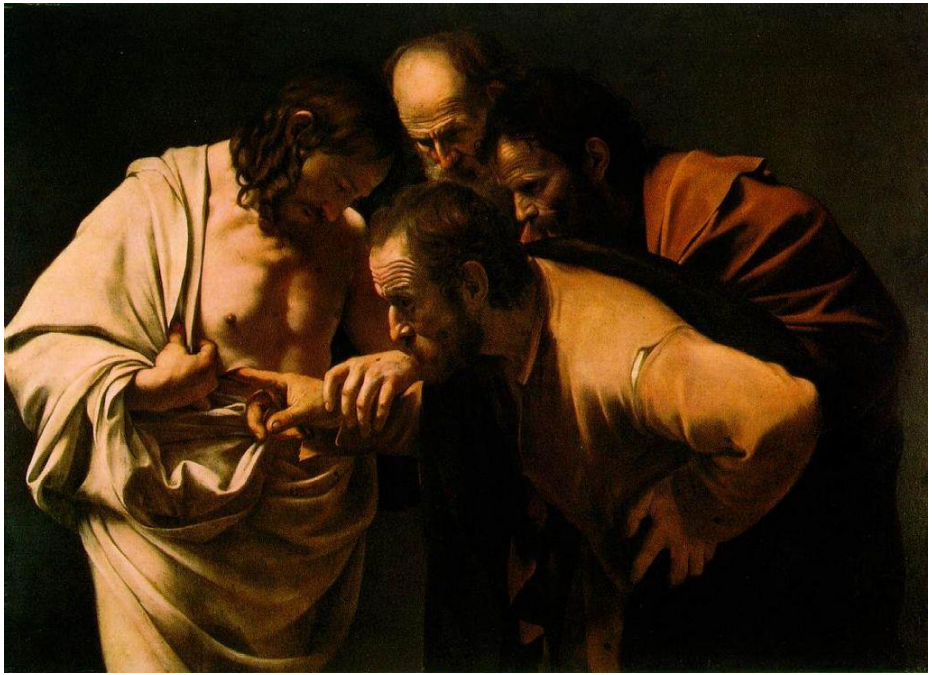
# Médecine fondée sur les preuves



*La crédulité de Saint Thomas*
*Michelangelo Merisi da Caravaggio (1571-1610)*

1. ***Le diabète est une situation à haut risque cardiovasculaire***

2. ***L'optimisation des FRCV et les traitements médicaux diminuent le risque CV du patient diabétique***

3. ***Les méthodes d'imagerie cardiaque non invasive (ischémie, anatomie calcium) ont une valeur pronostique démontrée***

# Croyance

*La croyance est l'acte d'admettre une idée, une opinion, ou une explication.*
***Si son exactitude est vérifiée par l'observation et l'expérience, elle cesse d'être une croyance et devient une connaissance.***

*Gustave le Bon (1841-1931)*

***La détection et le traitement***

***(médical ou interventionnel)***

***de la coronaropathie silencieuse***

***diminue la morbi-mortalité CV***

*La différence entre médecine fondée sur les preuves*

*et croyances ne tient parfois qu'à le valeur de p !*

RISQUE CV

# Evénements CV chez les diabétiques de type II

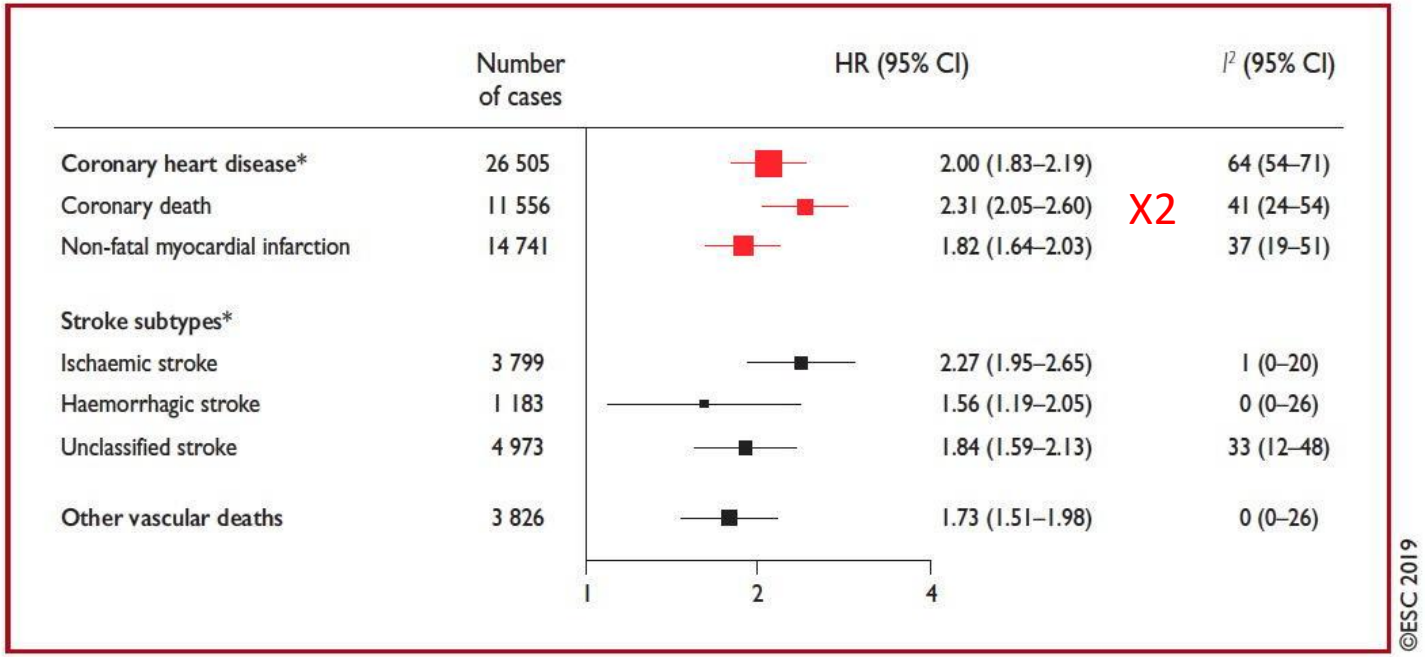
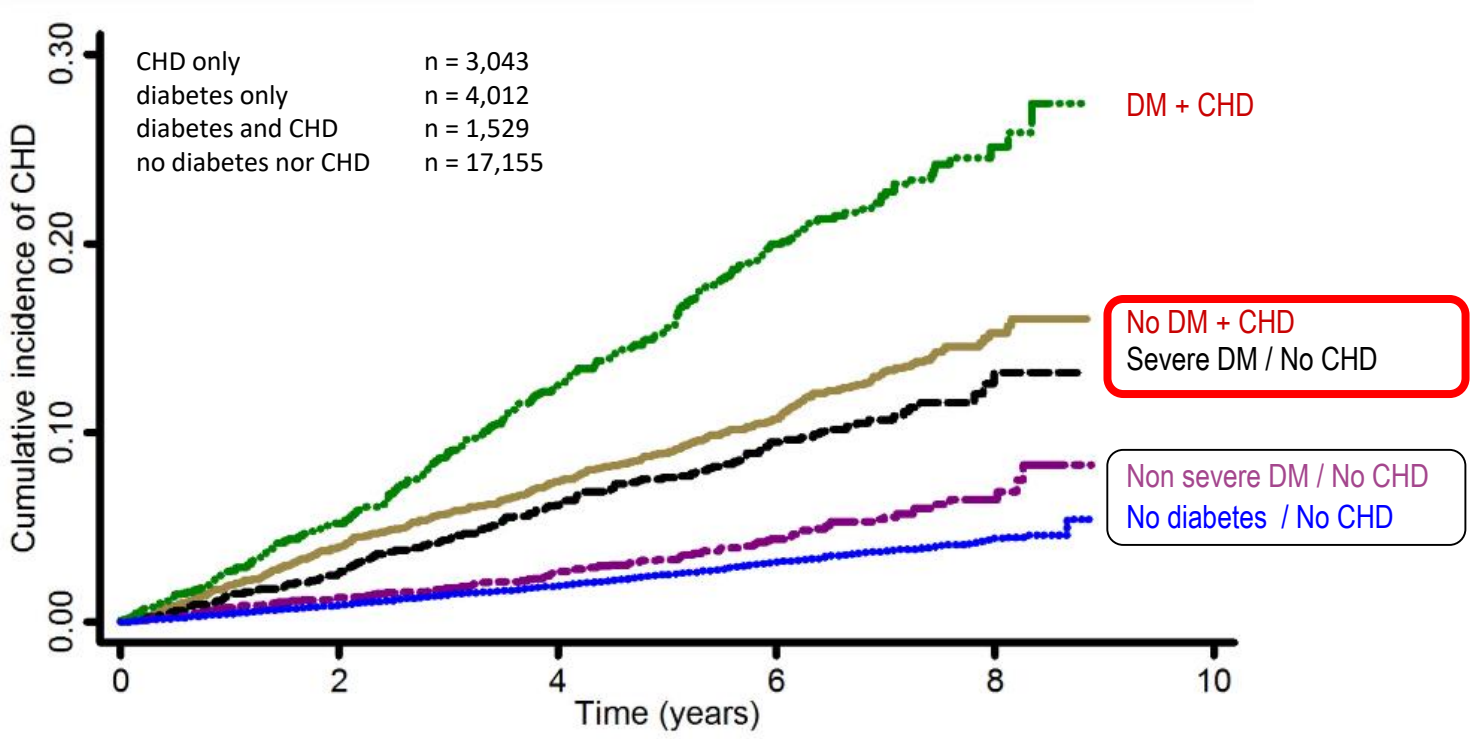



**Figure 1** Hazard ratios for vascular outcomes in people with vs. without diabetes mellitus at baseline, based on analyses of 530 083 patients. Reproduced with permission.[23] Hazard ratios were adjusted for age, smoking status, body mass index, and systolic blood pressure, and—where appropriate—stratified by sex and trial arm. The 208 coronary heart disease outcomes that contributed to the grand total could not contribute to the subtotals of coronary death or non-fatal myocardial infarction because there were <11 cases of these coronary disease subtypes in some studies. CI = confidence interval; HR = hazard ratio. [a]Includes fatal and non-fatal events.

Collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:22152222

RISQUE CV

# Le(s) risque(s) CV chez les diabétiques de type II




Mondesir FL et al Am Heart J 2016;181:43-5

RISQUE CV

# Définition du diabétique à haut risque CV

## SFC ALFEDIAM 2004

| | |
|---|---|
| High risk | Type 2 DM > 60 yrs<br>**and** > 10 yrs of evolution<br>**and** ≥ 1 target organ damage<br>Moderate to severe retinopathy<br>Macroproteinuria and/or renal failure<br>Peripheral vascular disease<br>**or** high level of associated risk factors |

## ESC 2019

| | |
|---|---|
| **Very high risk** | Patients with DM **and** established CVD<br>**or** other target organ damage[b]<br>**or** three or more major risk factors[c]<br>**or** early onset T1DM of long duration (>20 years) |
| **High risk** | Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor |
| **Moderate risk** | Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors |

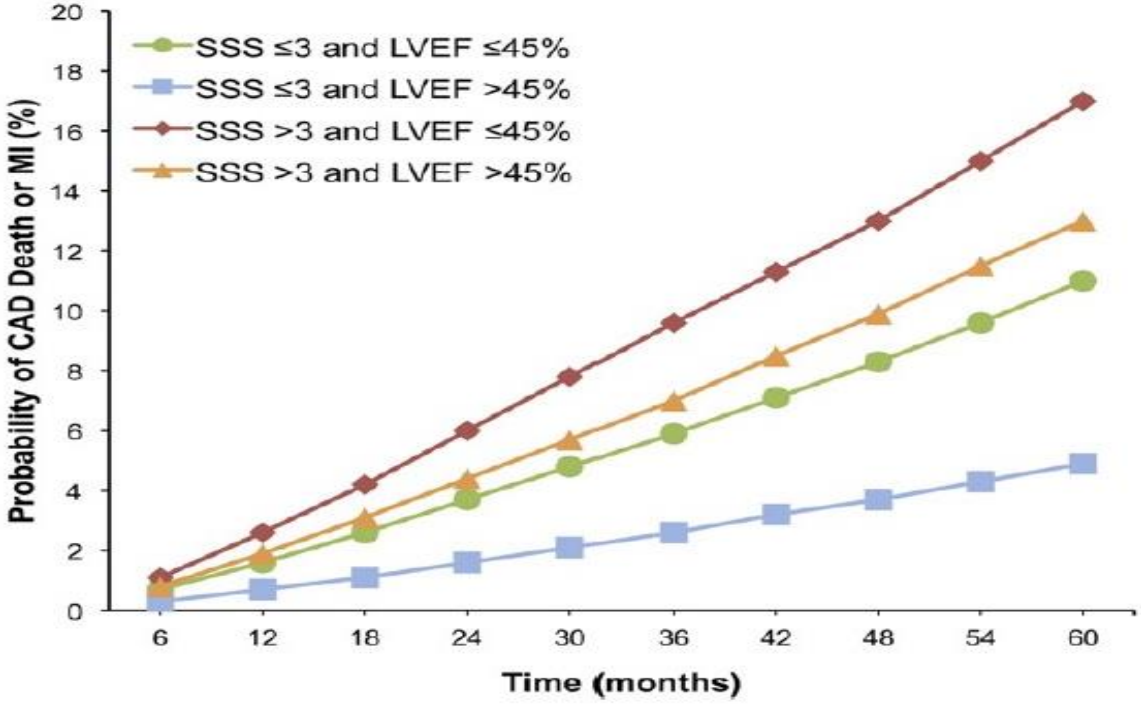
b: Proteinuria, or renal impairment, or LVH, or retinopathy.

c : Age, hypertension, dyslipidemia, smoking, obesity.

VALEUR PRONOSTIQUE DE L'IMAGERIE

# Imagerie de l'ischémie : TSM et ECHO

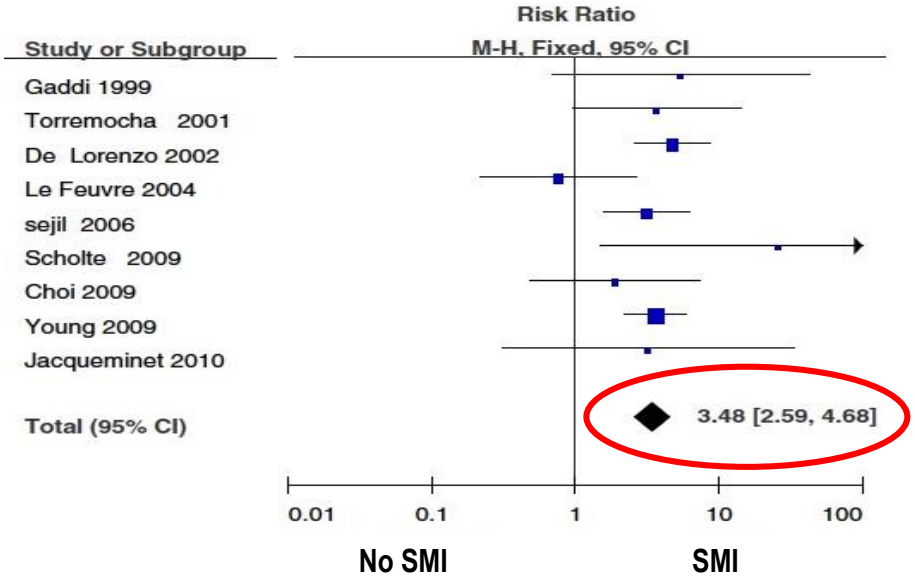
25+ ans d'expérience
25000+ patients
Suivi → 20 ans



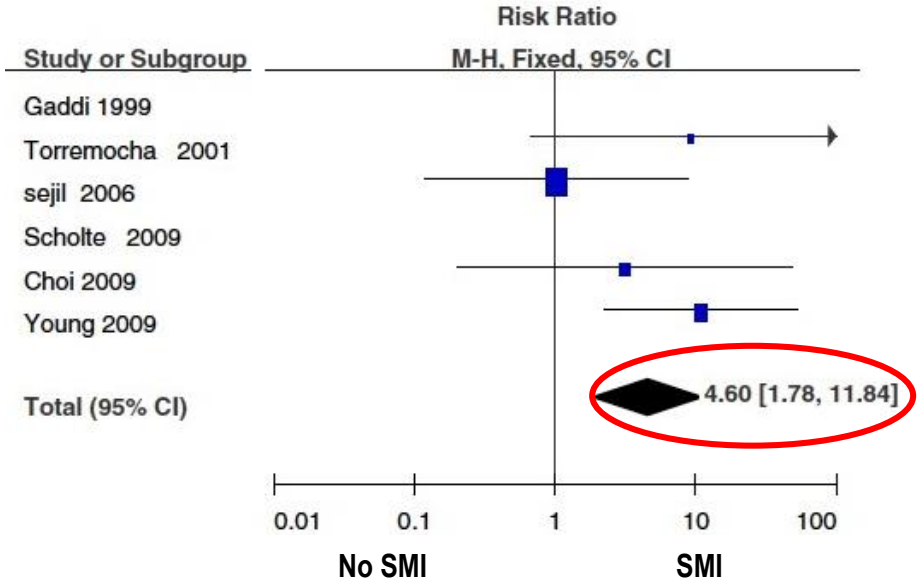

Acampa & al. Atherosclerosis 2013;227:307-12

# Imagerie de l'ischémie : TSM et ECHO

## MACCES



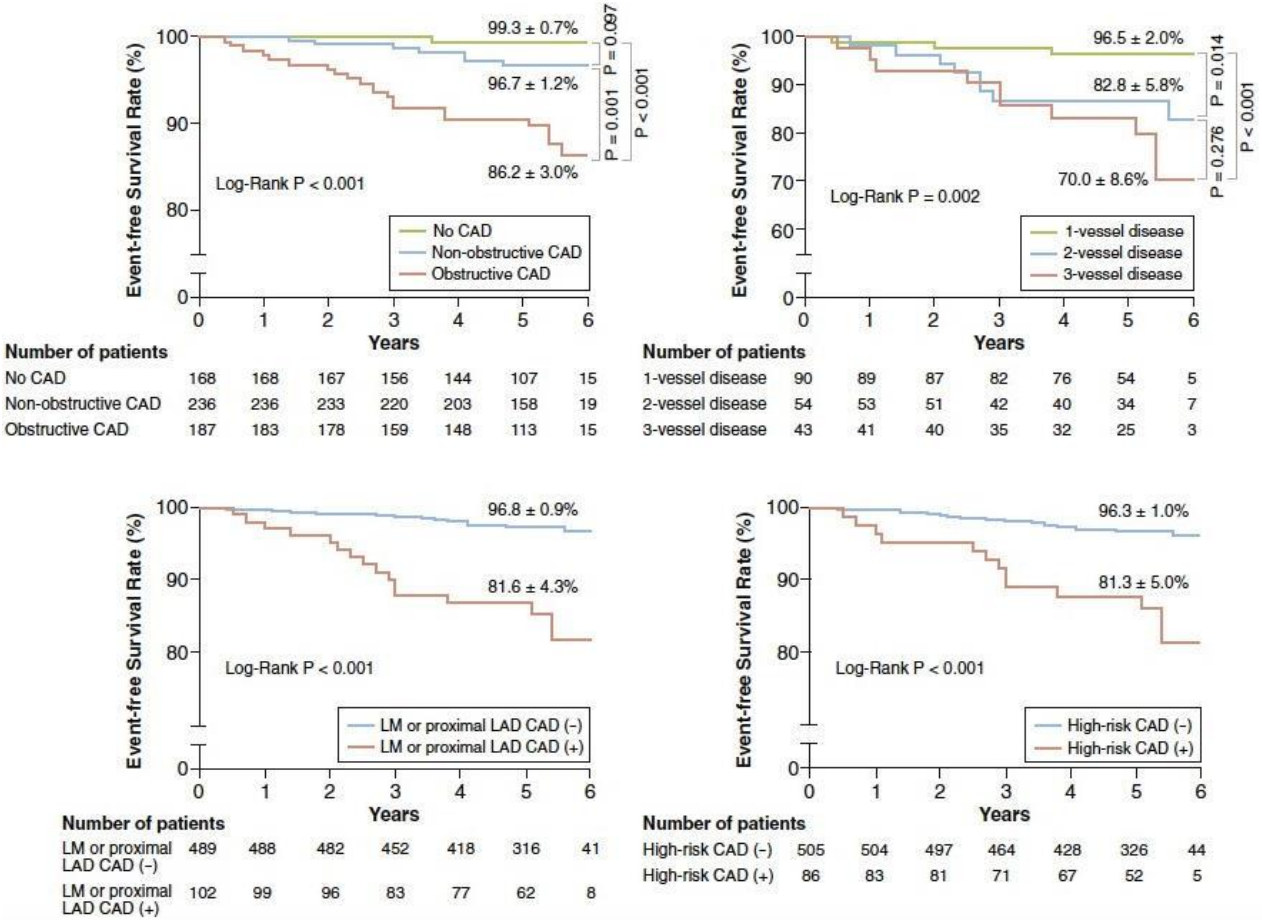

## Cardiac Death




Zhang & al. Diab Complic 2014;28:413–8

VALEUR PRONOSTIQUE DE L'IMAGERIE

# Imagerie anatomique non invasive

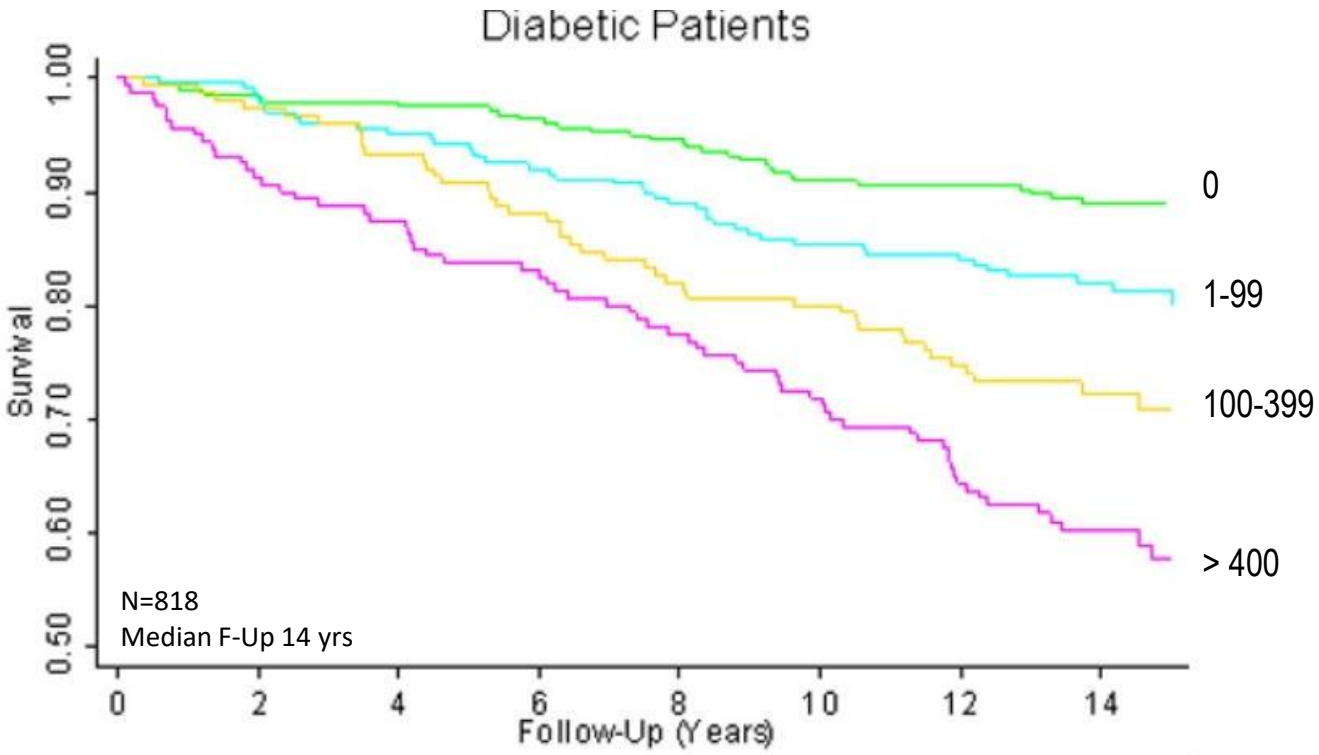



## Long-Term Prognostic Value of Coronary CT Angiography in Asymptomatic Type 2 Diabetes Mellitus

High risk patients
Diabetes 10 yrs
20% neuropathy
19% retinopathy
17% nephropathy
UKPDS 10 year-risk score19%

SE Huan & al. Am Coll Cardiol Img 2016;9:1292–300

# Imagerie du calcium : CAC-CT

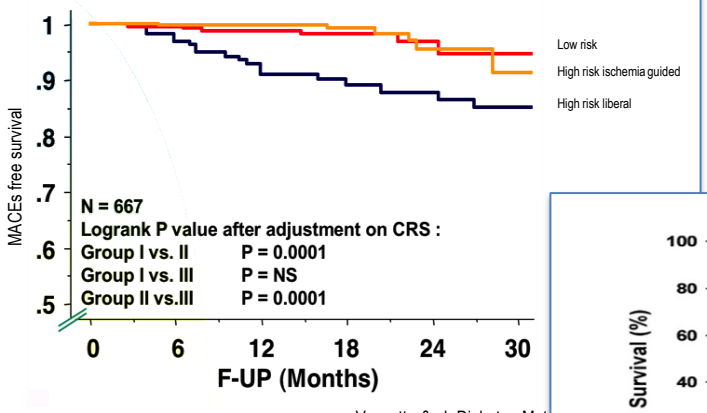



CAC provides incremental prognostic utility for prediction of mortality with a CAC=0 associated with reduced risk of death

Valenti & al. Circ Cardiovasc Imaging. 2016;9:online

STRATEGIES
DETECTION /
INTERVENTION

# Registres & analyses post-hoc encouragants




Vanzetto & al. Diabetes Meta

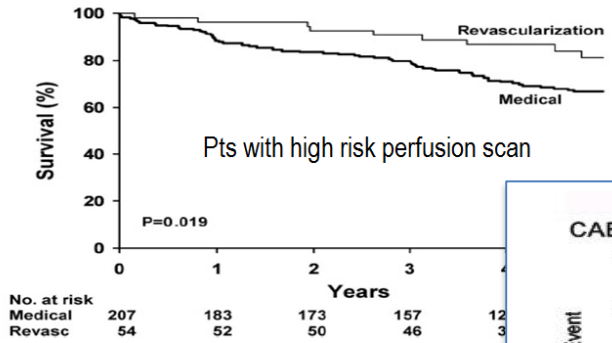
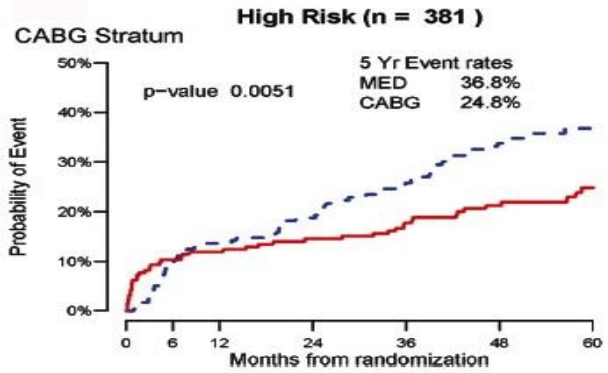



Figure 2. Survival of patients with high-risk perfusion
ties (SSS ≤47).

Soraja & al. Circulation. 2




Brooks & al. Circulation. 2012;126:2115-24

STRATEGIES DETECTION / INTERVENTION

# La désillusion des essais randomisés

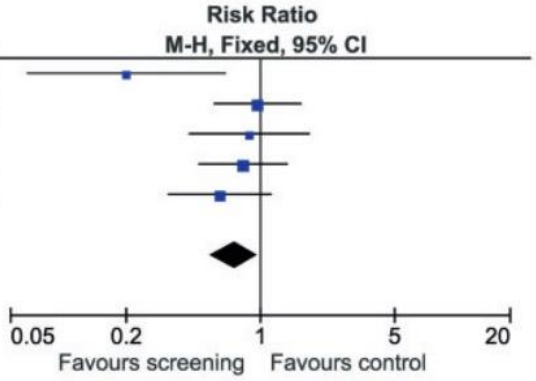
| Study/author | Faglia *et al.*[69] | DIAD[68] | DYNAMIT[64] | FACTOR-64[67] | DADDY-D[70] |
|---|---|---|---|---|---|
| Year of publication | 2005 | 2009 | 2011 | 2014 | 2015 |
| Patients (*n*) | 141 (+1)[a] | 1123 | 615 | 899 | 520 |
| Inclusion criteria | T2DM | T2DM | T2DM | T1DM or T2DM | T2DM |
| | 45–76 years | 50–75 years | 50–75 years | ♂ aged ≥50 years/ ♀ aged ≥55 years, DM for ≥3 years | 50–75 years |
| | ≥2 other CVRFs | | ≥2 other CVRFs | | CV risk ≥10% |
| | | | | | Sinus rhythm |
| | | | | | Able to do EET |
| Mean age (years) | 60.1 | 60.8 | 63.9 | 61.5 | 61.9 |
| Male sex (%) | 55.6 | 53.5 | 54.5 | 52.2 | 80.0 |
| Screening test | Stress echo | TSM | TSM ou EE | CTCA -CAC | EE |
| Positive screening test (%) | 21.1 | 5.9 moderate or large defects | 21.5 positive or uncertain | 11.9 moderate; 10.7 severe | 7.6 |
| Treatment strategy | ICA and cardiac follow-up if any test was positive | At the referring physician's discretion | According to the cardiologist's decision | Recommendation based on stenosis severity and CAC score | ICA if EET positive |
| ICA performed after positive test (%) | 93.3 | 15.2 | 55.9 | 47.3 | 85.0 |
| Mean follow-up (years) | 4.5 | 4.8 | 3.5 | 4.0 | 3.6 |
| Annual rate of major CEs (%) | 1.9 | 0.6 | 1.0 | 0.8 | 1.4 |
| Main results of screening | Significant ↓ of major and all CEs | NON SIGNIFICANT ↓ IN CARDIAC EVENTS | | | |

# Méta-analyses

| Study or Subgroup | Screening Events | Screening Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Faglia *et al.* | 3 | 71 | 15 | 71 | 13.7% | 0.20 [0.06, 0.66] | 2005 |
| DIAD | 26 | 561 | 27 | 562 | 24.7% | 0.96 [0.57, 1.63] | 2009 |
| DYNAMIT | 13 | 306 | 15 | 309 | 13.7% | 0.88 [0.42, 1.81] | 2011 |
| FACTOR-64 | 23 | 452 | 28 | 447 | 25.8% | 0.81 [0.48, 1.39] | 2014 |
| DADDY-D | 15 | 262 | 24 | 258 | 22.1% | 0.62 [0.33, 1.15] | 2015 |
| **Total (95% CI)** | | **1652** | | **1647** | **100.0%** | **0.73 [0.55, 0.97]** | |
| Total events | 80 | | 109 | | | | |

Heterogeneity: Chi² = 6.27, df = 4 (*P* = 0.18); I² = 36%

Test for overall effect: Z = 2.19 (*P* = 0.03)




Compared with the standard care, non-invasive CAD screening **significantly reduced cardiac events by 27%**, largely through reductions in non-fatal MIs, and HF hospitalisations.

*Clerc & al. Eur Heart J - CV Imaging. 2018;19: 838–84*

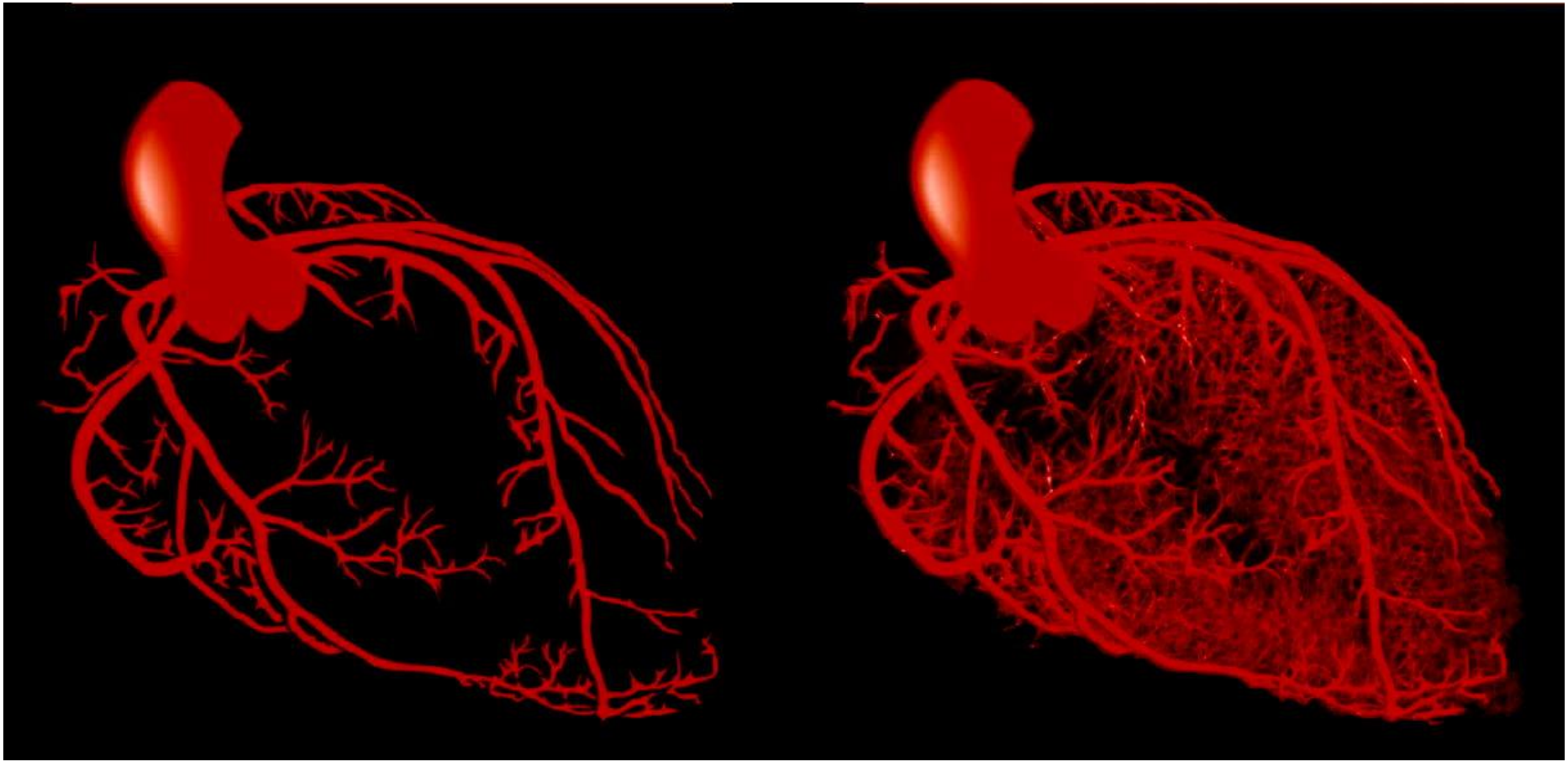
**Table 2** Results for myocardial infarction, revascularisation and heart failure of screening versus no screening

| Outcome | RR (95% CI) | Accrued population | Optimal sample size (RRR=40%) | Optimal sample size (RRR=20%) |
|---|---|---|---|---|
| Non-fatal myocardial infarction | 0.65 (0.41 to 1.02) | 3315 | 6154 | 17 495 |
| Heart failure | 0.60 (0.33 to 1.10) | 3174 | 10 990 | 49 352 |
| Revascularisations | 1.08 (0.83 to 1.41) | 3174 | 10 598 | 47 339 |

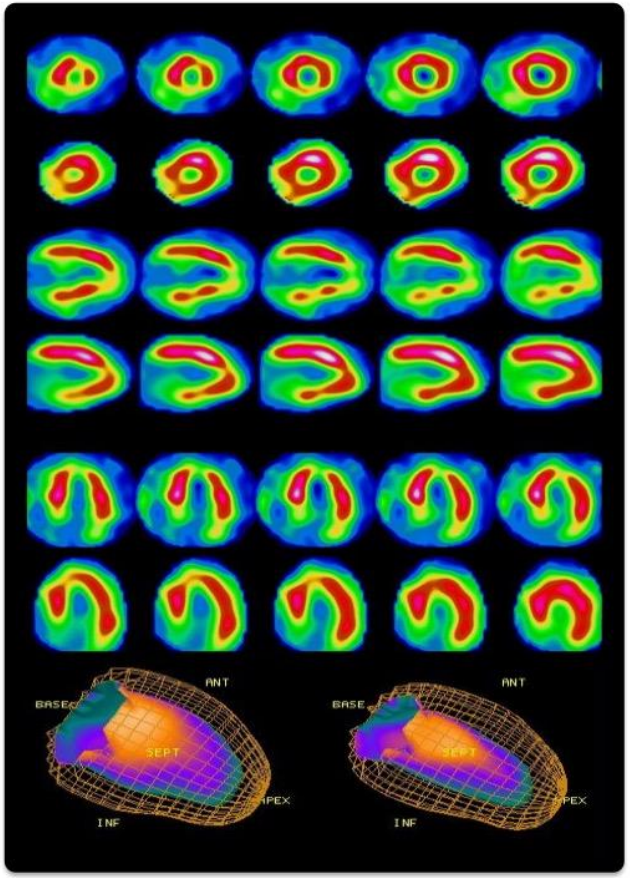
The present study support the ideas that asymptomatic type 2 DM patients **do dont warrant any CAD-screening**, avoiding unnecessary costs and patient distress.

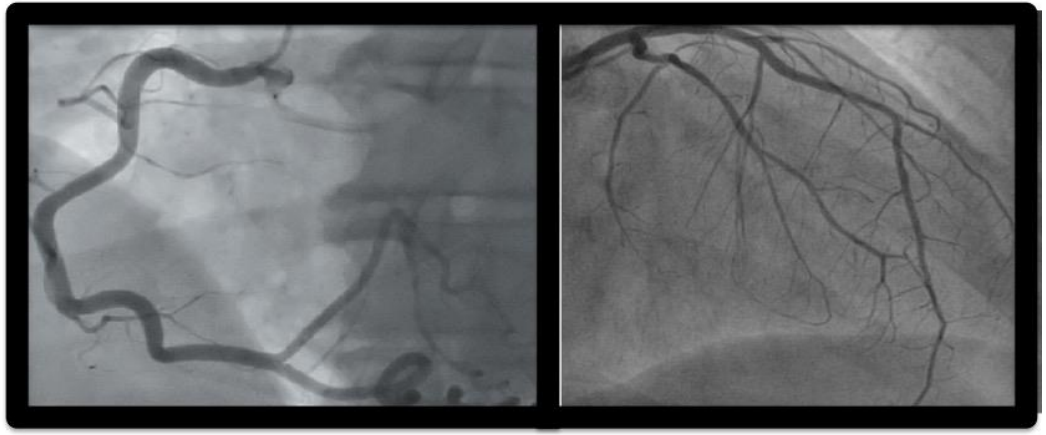
*Rados DV, et al. BMJ Open 2017;7:e015089*

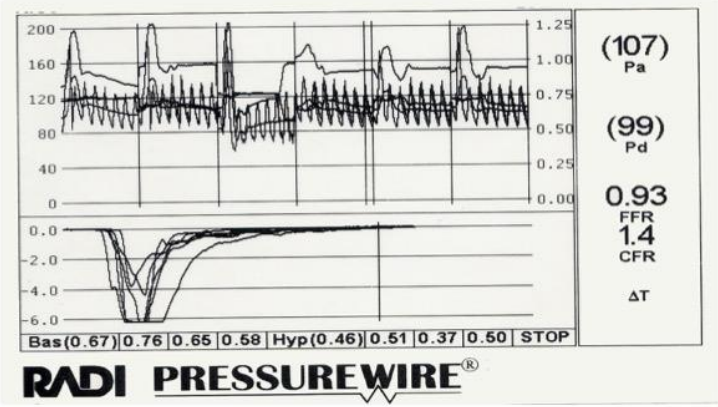
# Et en plus il y a la microcirculation !



# Atteinte microcirculatoire du diabète



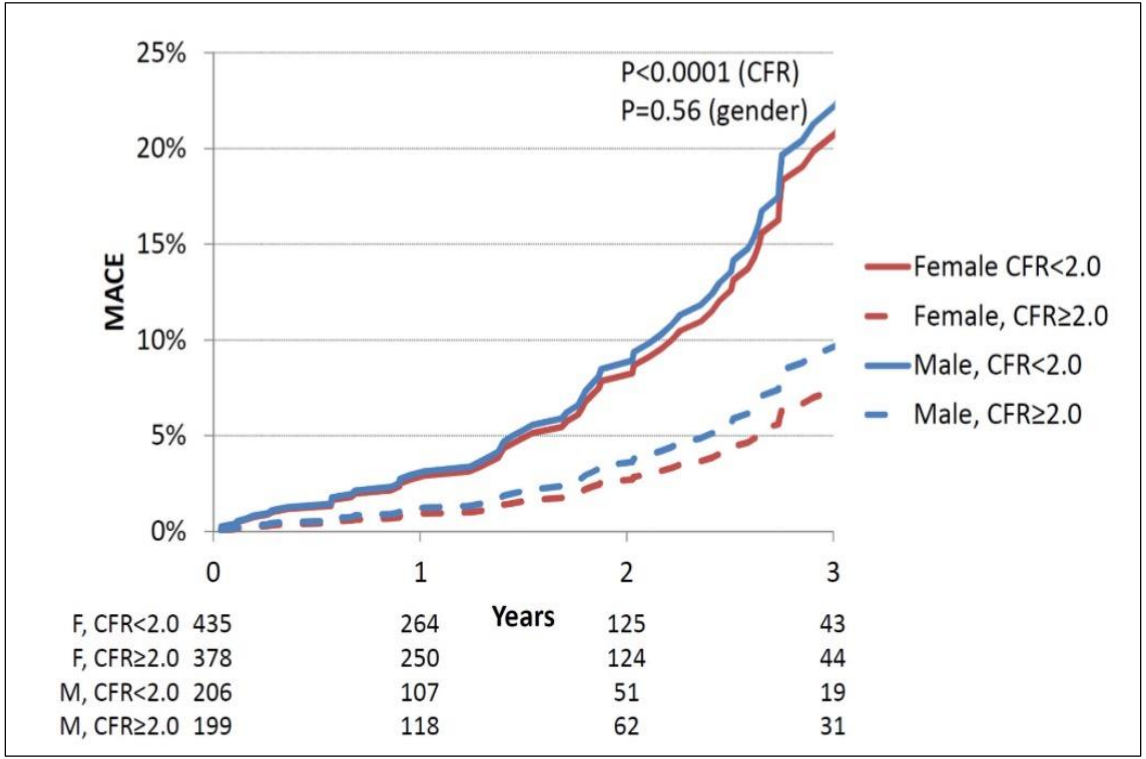



FFR 0.93

CFR 1.40

IMR 45

# Valeur pronostique de l'atteinte microcirculatoire




Murthy & al. Circulation. 2014;129: 2518–2527

Et maintenant je fais quoi…?

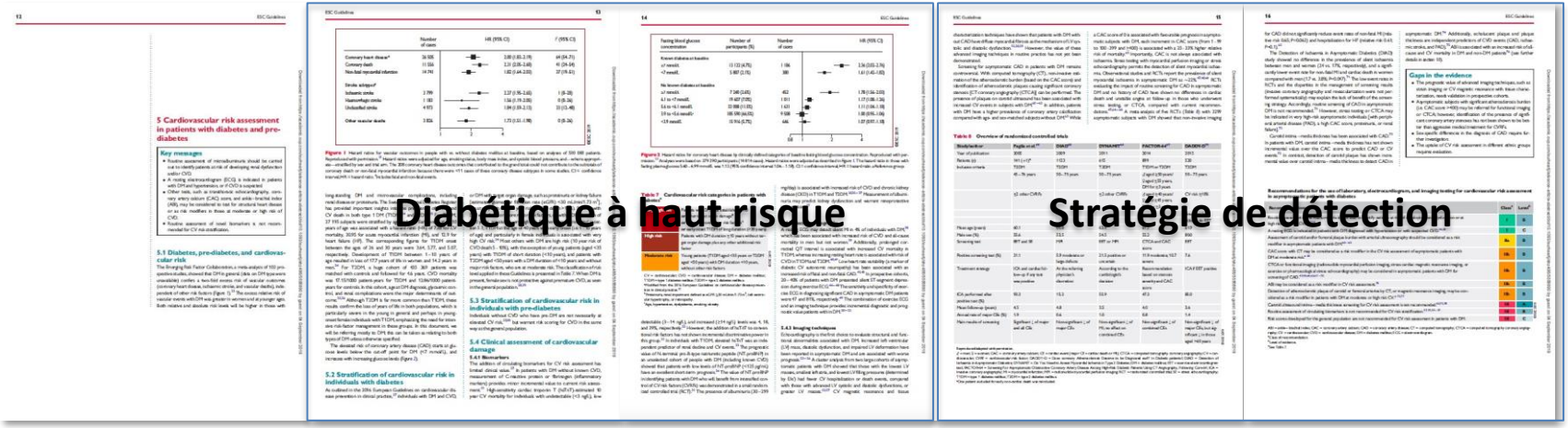
ESC 2019 GUIDELINES

# Recommandations ESC 2019

## 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

**The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)**

70 pages, 579 références bibliographiques



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## Gaps in the evidence

- Asymptomatic subjects with significant atherosclerosis burden (i.e. CAC score >400) may be referred for functional imaging or CTCA; however, identification of the presence of significant coronary artery stenoses has not been shown to be better than aggressive medical treatment for CVRFs.

## CV risk assessment

| | |
|---|---|
| Resting ECG is recommended in patients with DM with hypertension or suspected CVD | I A |
| Carotid or femoral ultrasound should be considered for plaque detection as CV risk modifier | II A |
| Screening for CAD with coronary CT angiography and functional imaging may be considered<br>CAC scoring may be considered as risk modifier<br>ABI may be considered as risk modifier | II B |
| Carotid ultrasound intima–media thickness for CV risk is not recommended | III |

PROPOSITION DE STRATÉGIE

# Coroscan en premier pour le dépistage ???

## Impact pronostic de la réalisation d'un coro-scanner : méta-analyse

Comparative safety and effectiveness of coronary computed tomography: Systematic review and meta-analysis including 11 randomized controlled trials and 19,957 patients

| Study (year) | Patients | Setting | Comparison |
|---|---|---|---|
| ACRIN-PA (2012) | 1370 | Acute chest pain | CoroCT vs standard care |
| BEACON (2016) | 500 | Acute chest pain | CoroCT vs standard care |
| CT-COMPARE (2014) | 562 | Acute chest pain | CoroCT vs exercise stress ECG |
| CT-STAT (2011) | 699 | Acute chest pain | CoroCT vs MPS |
| FACTOR-64 (2014) | 900 | Screening | CoroCT vs standard care |
| Goldstein (2007) | 197 | Acute chest pain | CoroCT vs standard care |
| Min (2012) | 180 | Suspected CAD | CoroCT vs MPS |
| PROMISE (2015) | 10,003 | Suspected CAD | CoroCT vs functional testing |
| PROSPECT (2015) | 400 | Acute chest pain | CoroCT vs MPS |
| ROMICAT-II (2012) | 1000 | Acute chest pain | CoroCT vs standard care |
| SCOT-HEART (2015) | 4146 | Suspected CAD | CoroCT vs standard care |

| Study (year) | Age | Female | DM | HTN | Dyslip | Smoking | Prior CHD |
|---|---|---|---|---|---|---|---|
| FACTOR-64 (2014) | 62 | 47% | 100% | 66% | 63% | 16% | 0% |
| Min (2012) | 58 | 51% | 22% | 61% | 57% | 51% | 0% |
| PROMISE (2015) | 61 | 53% | 21% | 65% | 68% | 51% | 0% |
| SCOT-HEART (2015) | 57 | 44% | 11% | 34% | 53% | 53% | 9% |

| | Screening | |
|---|---|---|
| End point | RR | [95%CI] |
| Coronary angio. | **2.68** | [1.62-4.08] |
| Coronary revasc. | **2.83** | [1.56-5.12] |
| † or MI | **0.84** | [0.49-1.45] |

Nudi & al. Int J Cardiol 2016;222:352-8

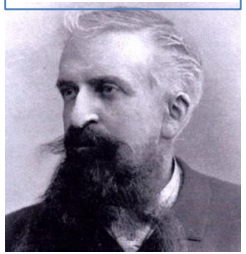
**PROPOSITION DE STRATÉGIE**

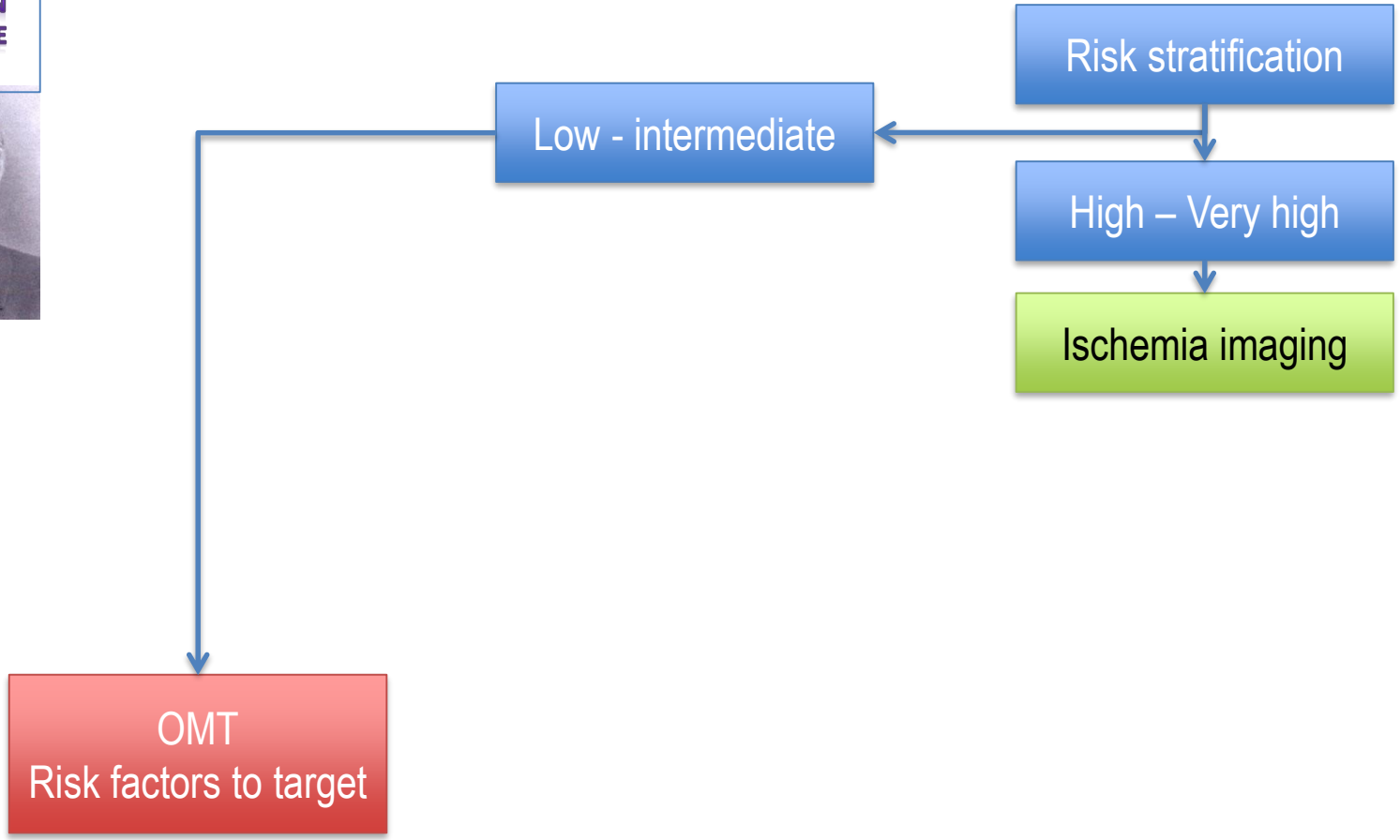
Diabetes

↓

OMT
Risk factors to target

**PROPOSITION DE STRATÉGIE**





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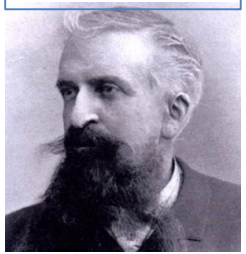

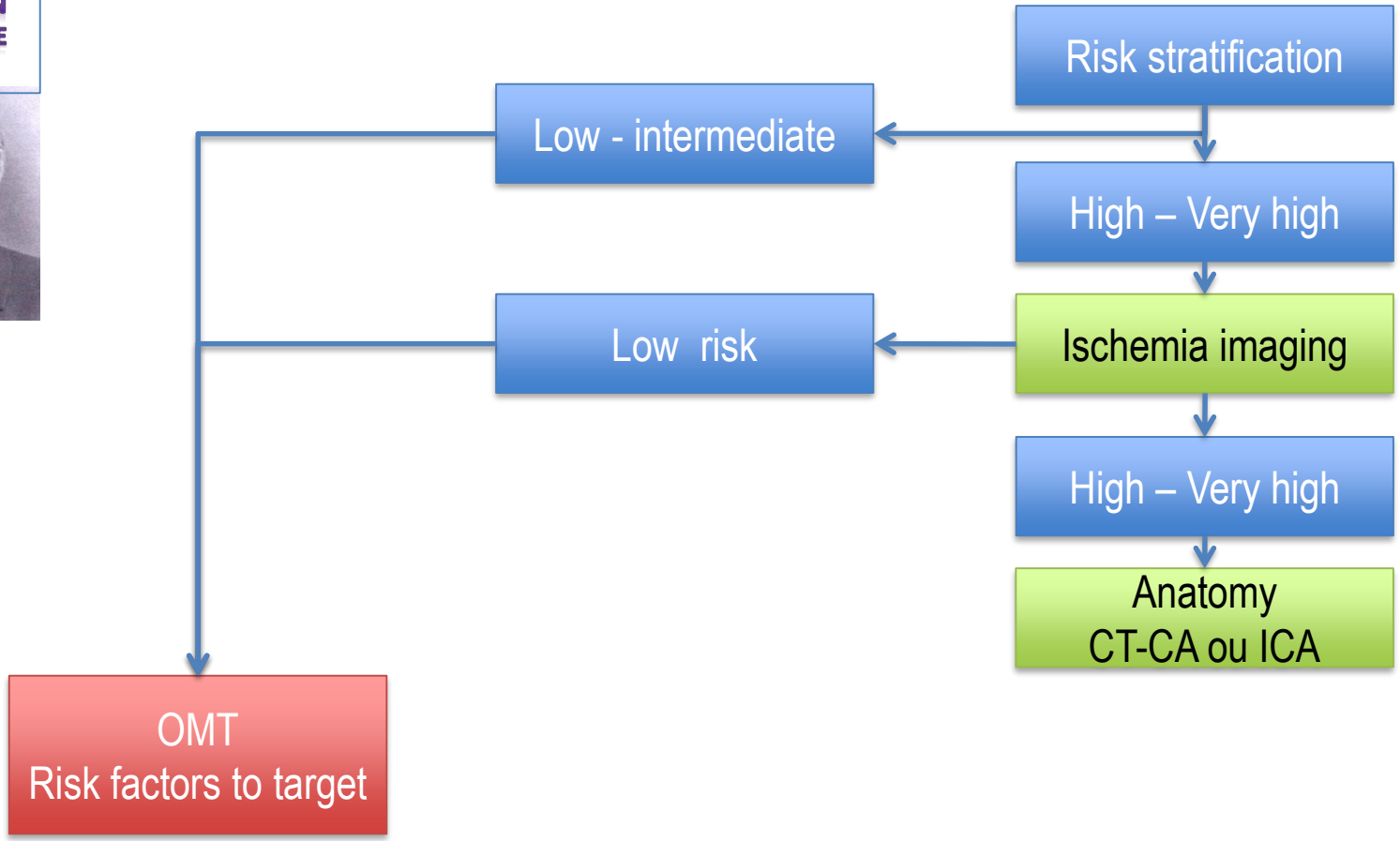

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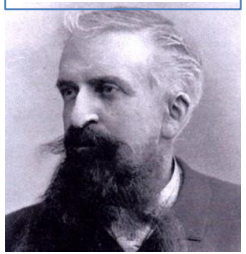

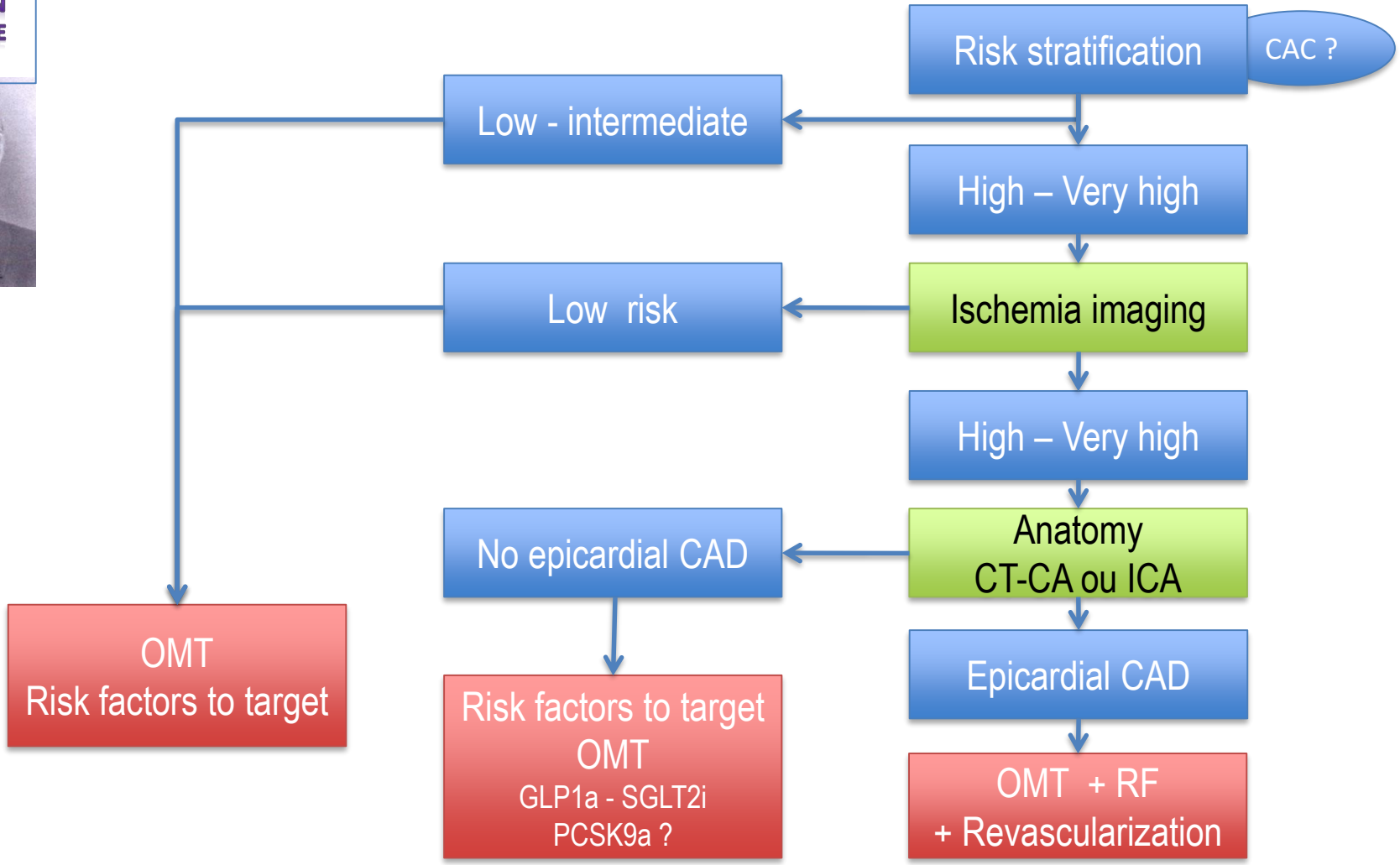

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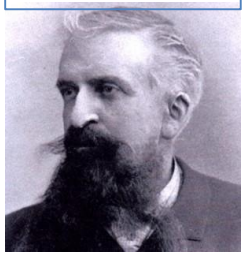

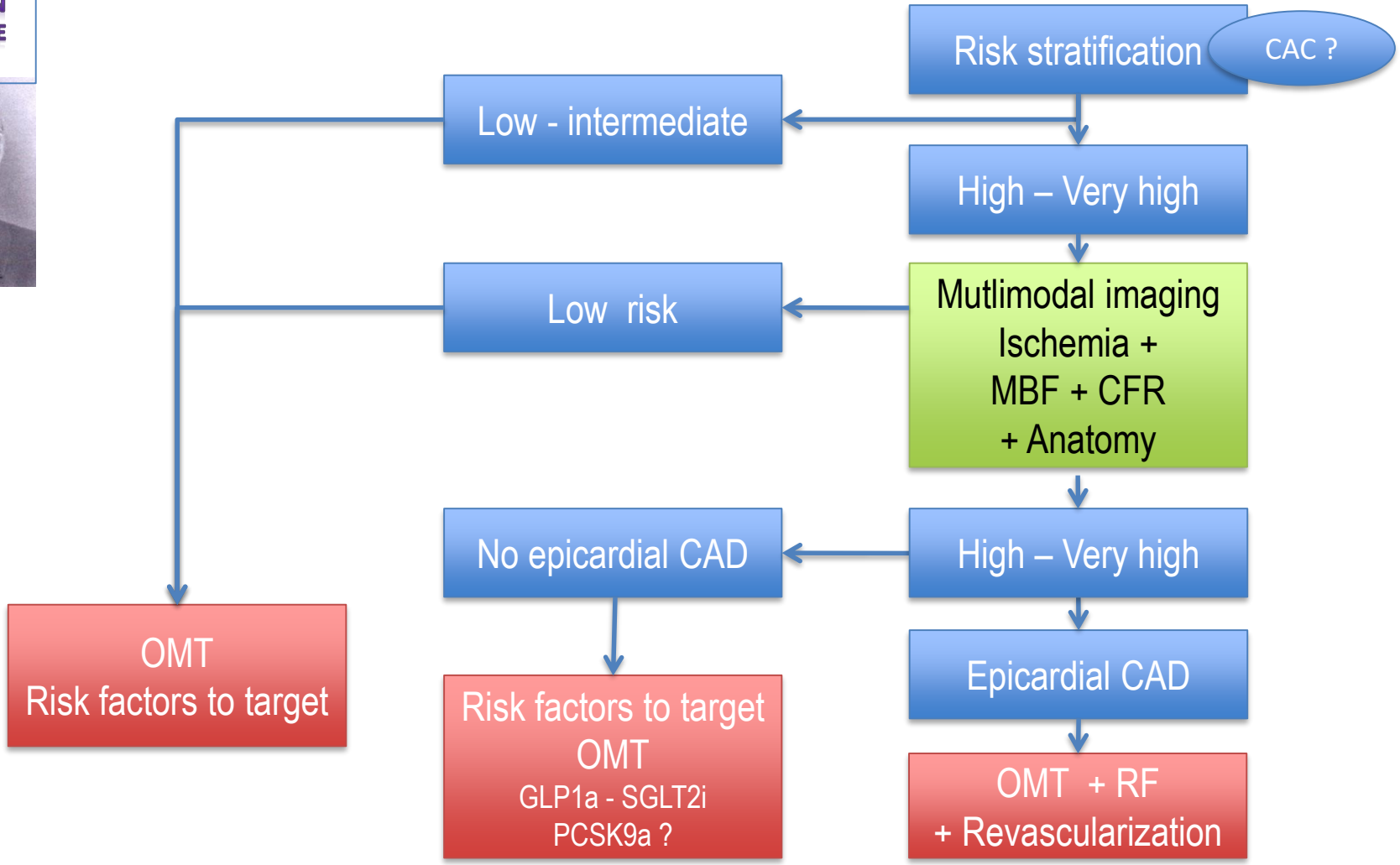

# Merci de votre attention !