Cardiologie et Maladie rénale chronique

Cardiopathie ischémique

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Hôpitaux Universitaires SAINT-LOUIS LARIBOISIÈRE FERNAND-WIDAL

Inserm

Université Paris Cité

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Liens d'intérêt

- Consulting and lecture fees:
  - Astra Zeneca
  - Bayer
  - Bristol-Myers Squibb (BMS) – Pfizer
  - Vifor Pharma
  - Novartis
  - Boehringer Ingelheim
  - Amarin corporation
  - Siemens Healthineers (France, Global)
  - GE Healthcare (France)
  - MEDIS imaging
  - Hexacath

- Research grants:
  - Servier
  - Bayer

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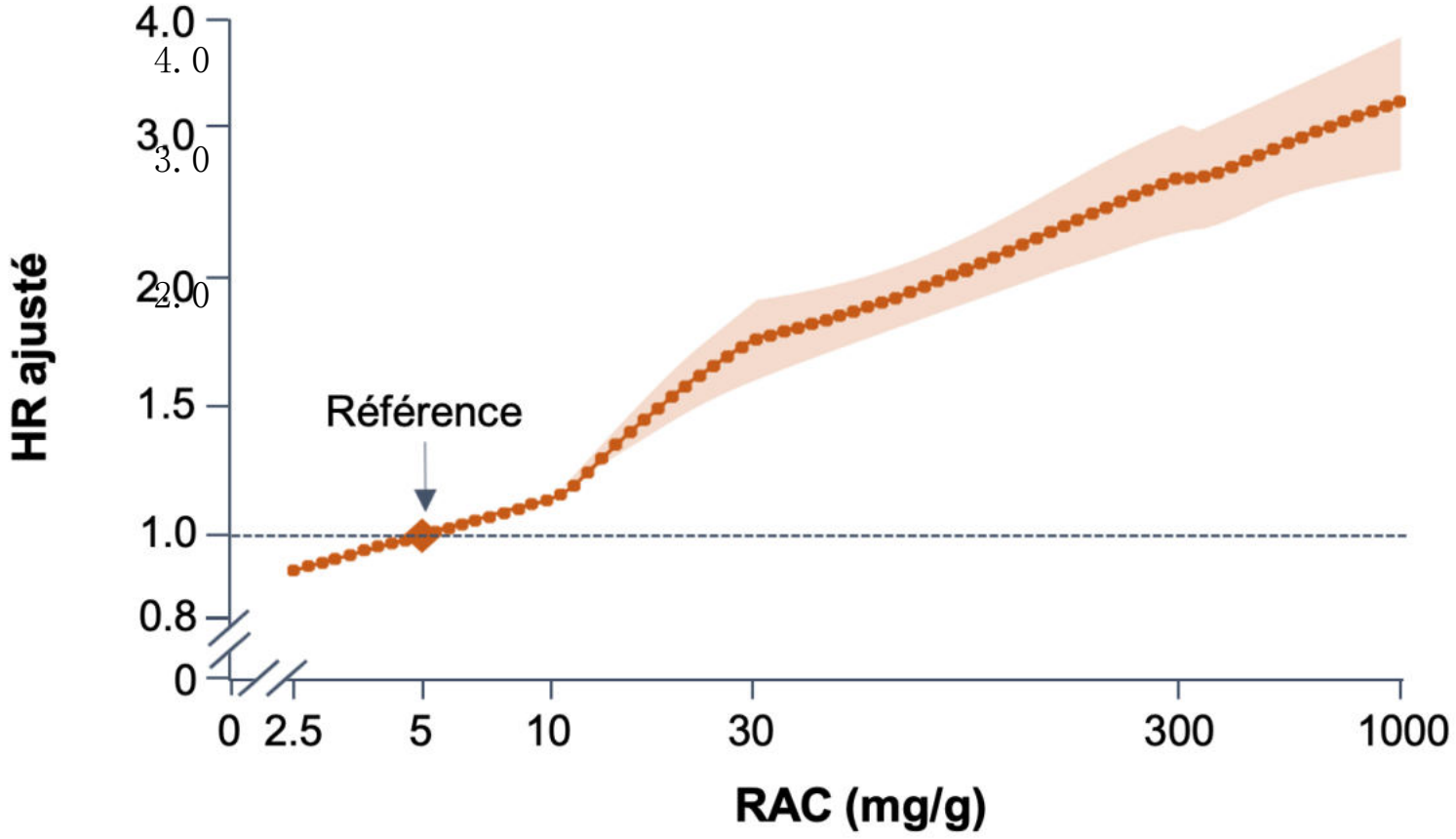
Problématique

Chronic Kidney Disease Prognosis Consortium: 637 315 patients without known CVD from 24 cohorts (F/U=5 years)



RAC: ratio albuminurie/créatininurie

Matsushita K, et al. Lancet Diabetes Endocrinol 2015

Coronary artery disease in Asymptomatic CKD patients

Silent ischemia and Unrecognized myocardial infarction

- **3 main risk factors** of silent ischemia or unrecognized myocardial infarction:
  - Diabetes mellitus
  - Hypertension
  - Chronic Kidney disease → ***silent ischemia in 10–25 % of patients!***

Arenja N et al. Prevalence, extent, and independent predictors of silent myocardial infarction. Am J Med. 2013
Kannel WB et al. Incidence and prognosis of unrecognized myocardial infarction. Framingham study. NEJM 1984
Valensi P et al. Prevalence, incidence, predictive factors and prognosis of silent myocardial infarction. ACVD 2011

3 Ways to Detect CAD

- **Coronary plaque / calcification**
- **Inducible myocardial ischemia**
- **Unrecognized myocardial infarction**

Indications to detect CAD

European Heart Journal (2016) 37, 2315–2381
doi:10.1093/eurheartj/ehw106

JOINT ESC GUIDELINES

2016 European Guidelines on cardiovascular disease prevention in clinical practice

The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)

Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)

Circulation

ACC/AHA CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

1. Angor typique ou atypique
2. ECG de repos suggérant une ischémie ou un infarctus myocardique
3. Athérosclérose carotidienne ou artériopathie des membres inférieurs
4. Sédentarité chez un sujet de plus de 35 ans présentant un deuxième facteur de risque et désirant reprendre une activité physique
5. Présence d'au moins deux facteurs de risque parmi :
   - Dyslipidémie
   - HTA
   - Tabagisme actif
   - Histoire familiale de coronaropathie précoce
   - Présence d'une micro- ou macroalbuminurie
   - Obésité abdominale
   - Age supérieur à 55 ans
   - Sédentarité

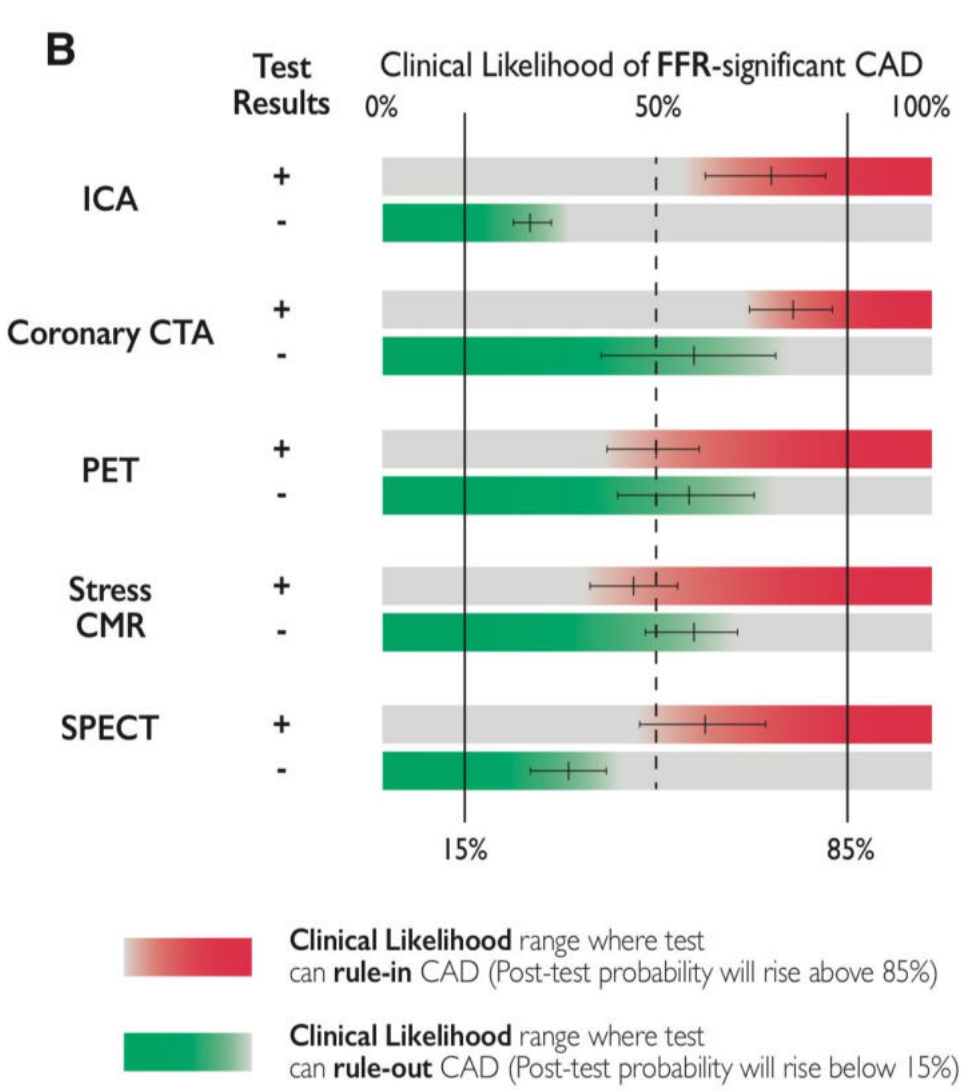
« Coronary plaque »
to detect CAD

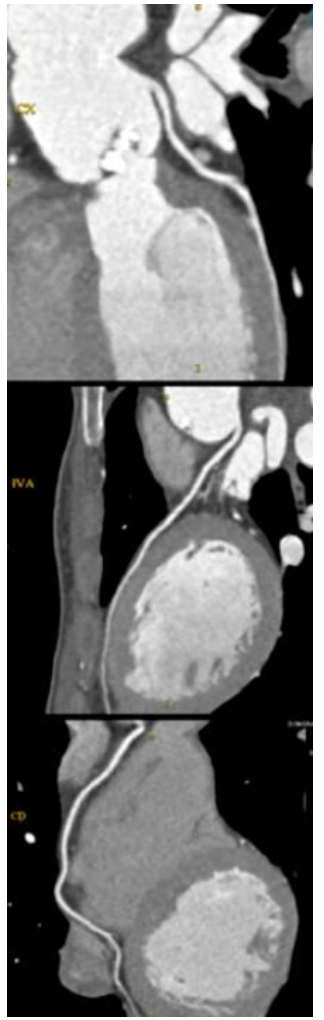
Coronary CT angiography

VPN = 97 %

Table 12 Characteristics of tests commonly used to diagnose the presence of coronary artery disease

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG [a, 91, 94, 95]	45–50	85–90
Exercise stress echocardiography[96]	80–85	80–88
Exercise stress SPECT[96, 99]	73–92	63–87
Dobutamine stress echocardiography[96]	79–83	82–86
Dobutamine stress MRI[b, 100]	79–88	81–91
Vasodilator stress echocardiography[96]	72–79	92–95
Vasodilator stress SPECT[96, 99]	90–91	75–84
Vasodilator stress MRI[b, 98, 100–102]	67–94	61–85
Coronary CTA[c, 103–105]	95–99	64–83
Vasodilator stress PET[97, 99, 106]	81–97	74–91



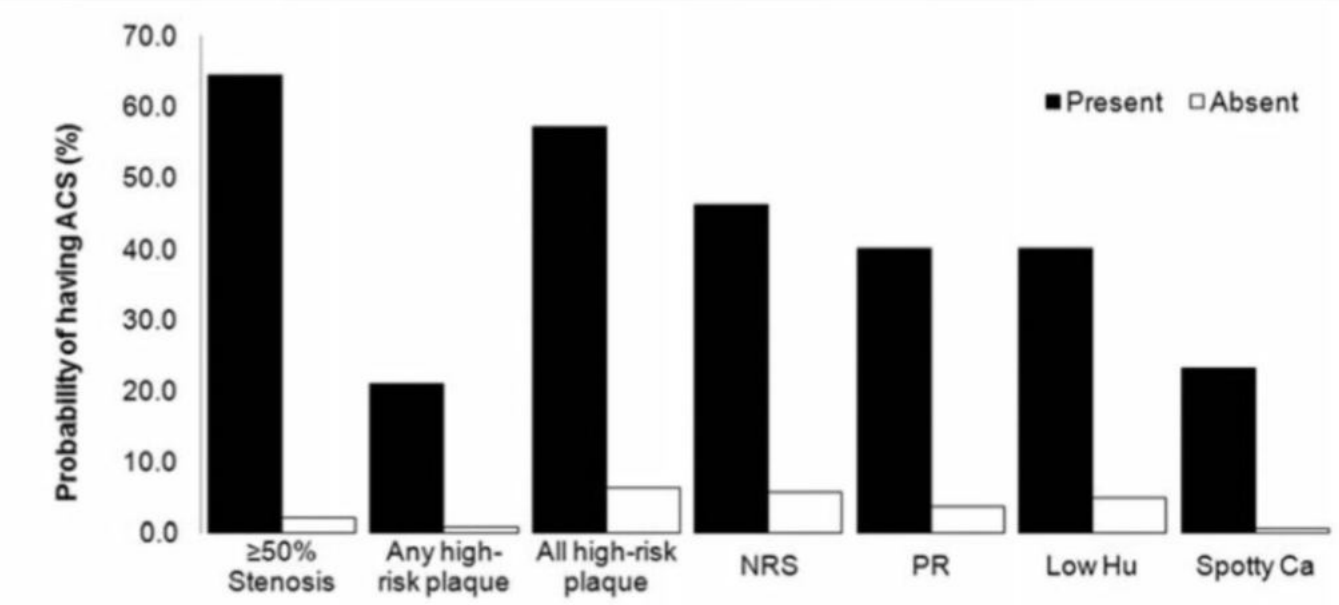


ESC Guidelines CAD, EHJ 2019

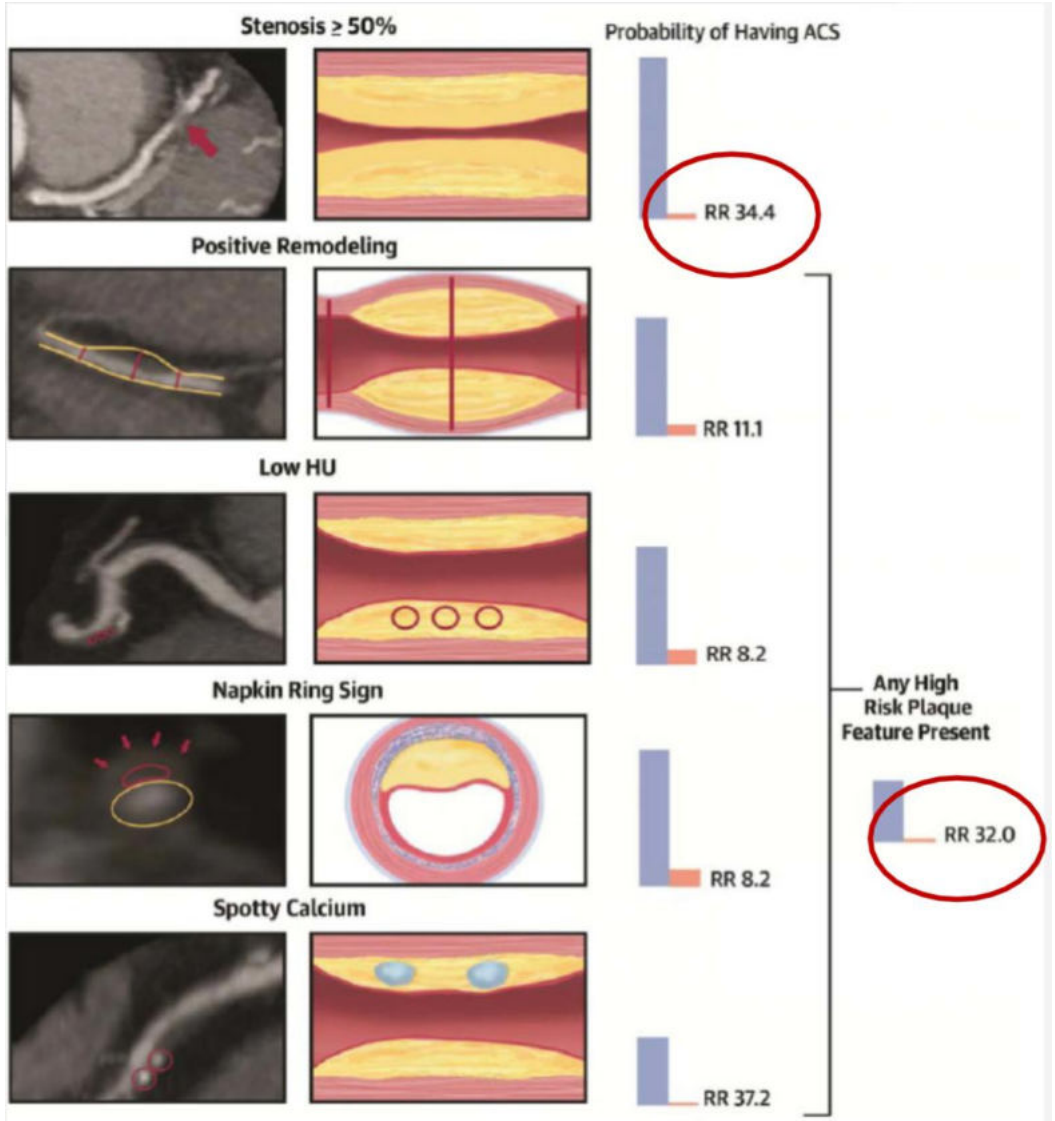
Coronary CT: Plaque Vulnerabilty

Coronary CT Angiography Predicts Acute Coronary Syndromes Independent of Significant Stenosis in Acute Chest Pain

Results From the ROMICAT-II



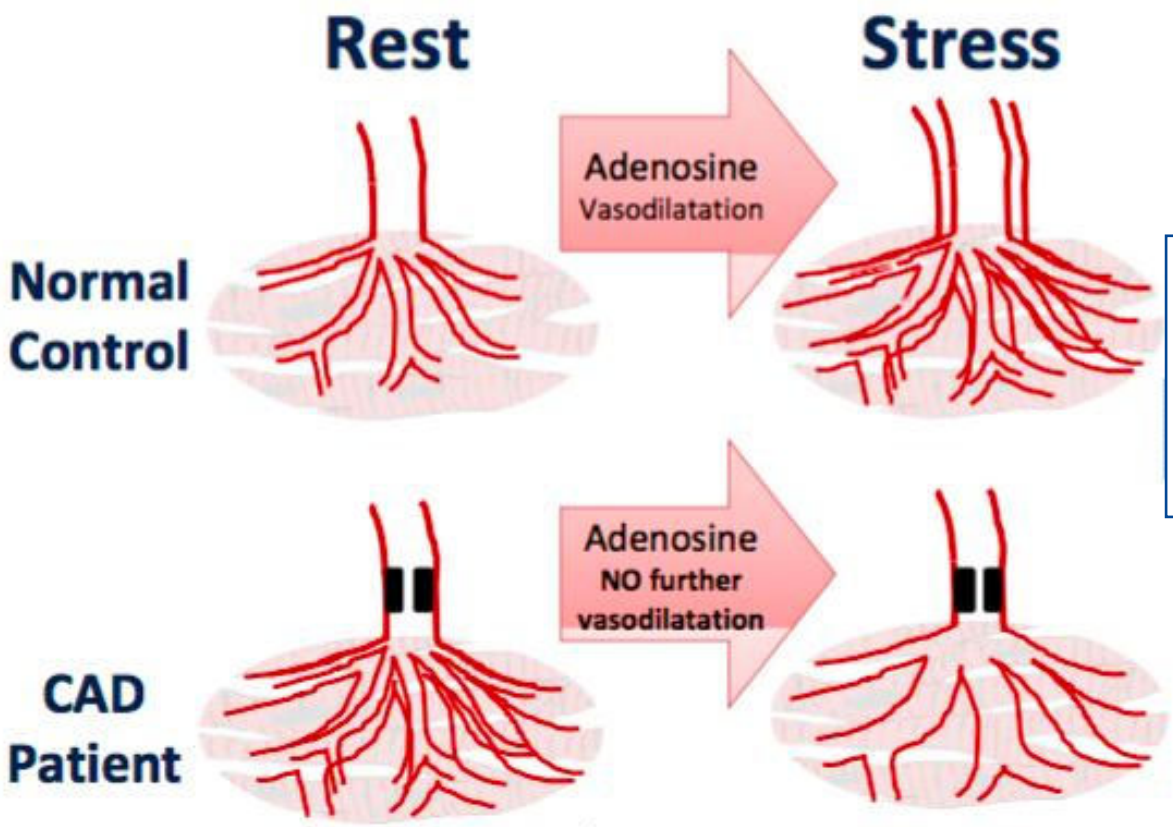
	≥50% Stenosis	Any high-risk plaque	All high-risk plaque	NRS	PR	Low Hu	Spotty Ca
Relative Risk	34.4	32.0	9.0	8.2	11.1	8.2	37.2
95% CI	(16.7-70.7)	(7.8-131.2)	(5.1-16.0)	(4.7-14.5)	(6.2-20.1)	(4.7-14.5)	(9.1-152.7)
P-Value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001



Truong QA. *et al.* Circulation 2013

« Inducible myocardial ischemia » to detect CAD

Test non-invasifs de stress



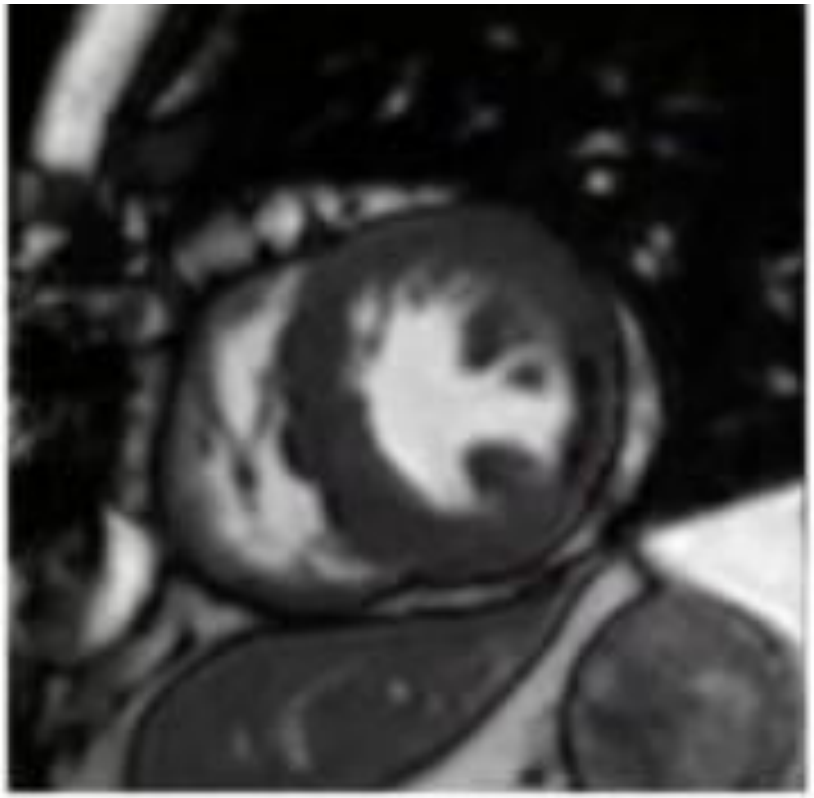
Vasodilatation globale et homogène

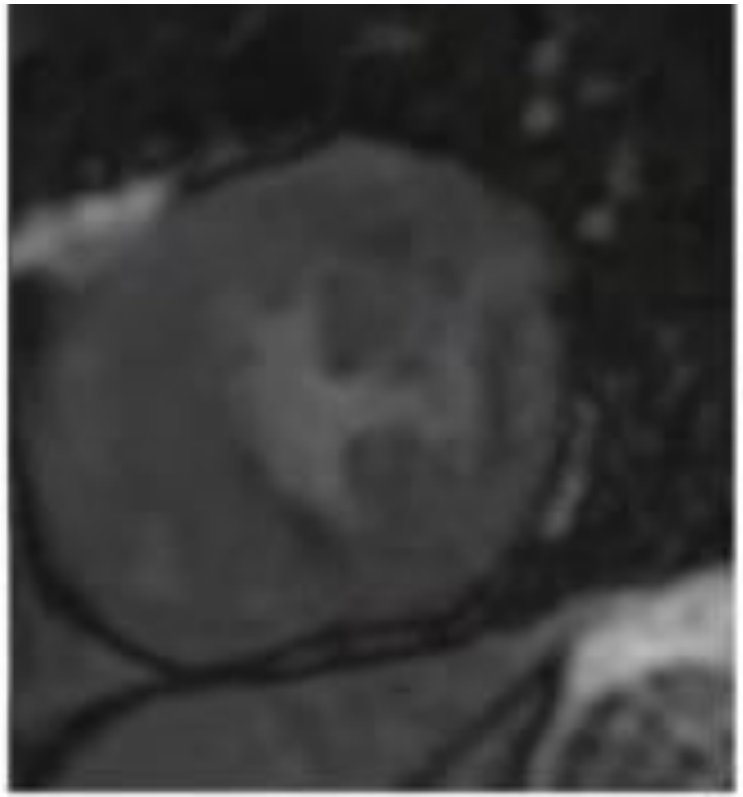
Vasodilatation compensatrice au repos en aval de la sténose

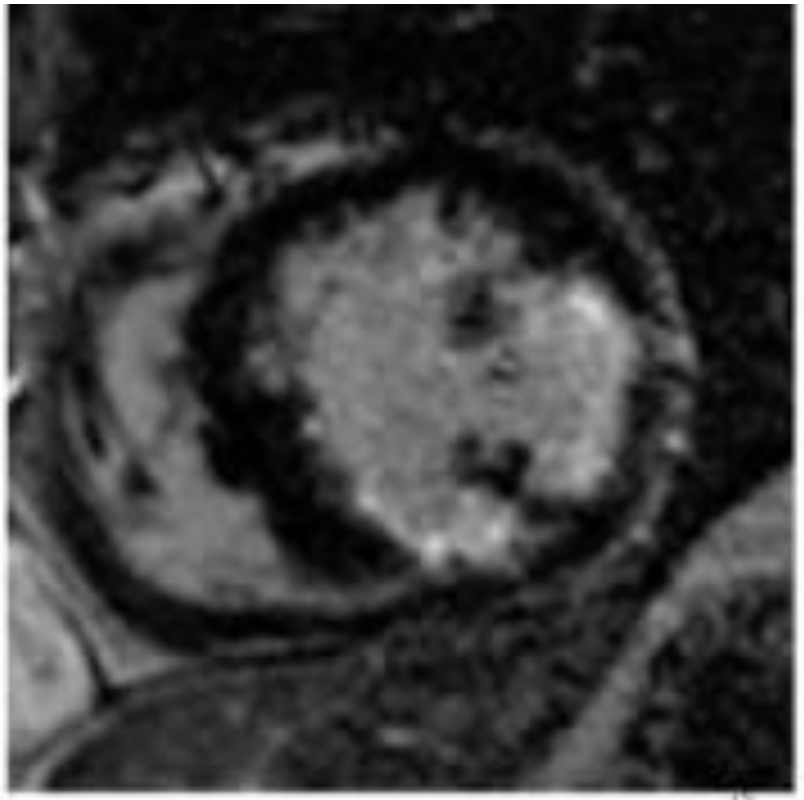
Vasodilatation limitée en aval de la sténose
(< importante que les territoires normaux)

ECG d'effort
Scintigraphie de perfusion ou TEP scan
Échocardiographie de stress
IRM cardiaque de stress

Stress CMR







Function

Perfusion

Scar

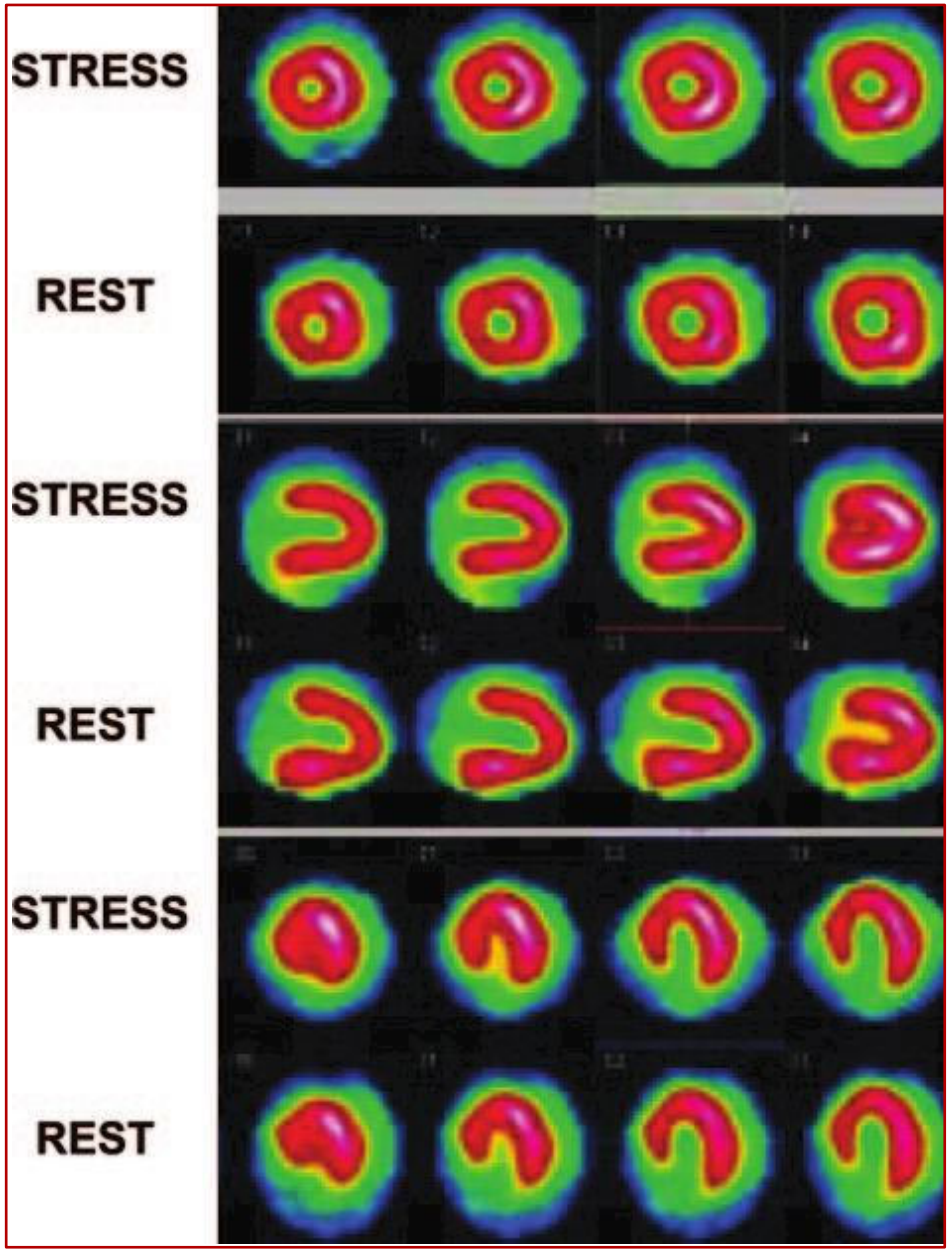
Sven Plein. Cardiac MRI, What the cardiologist needs to know, **ESC 2017**

Case report

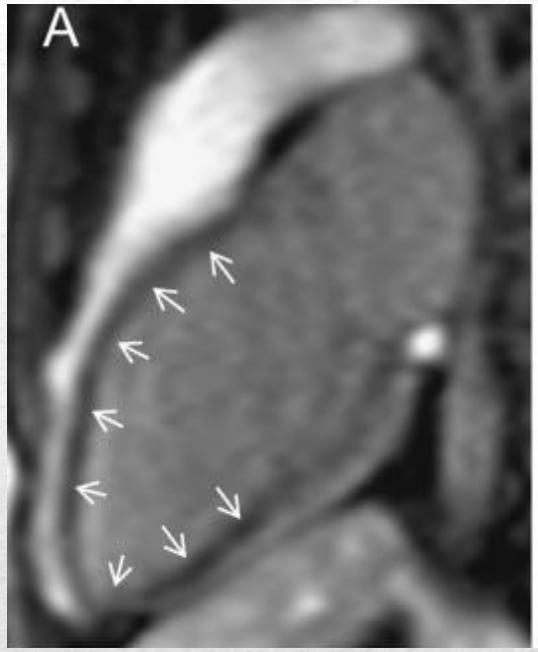
68-year-old man

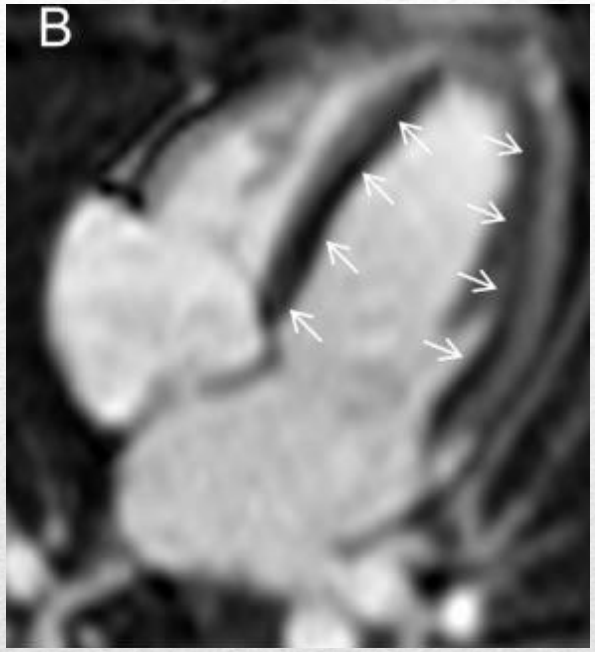
- **CKD** with **GFR= 44** ml/min
- **Chest pain** for 4 months
- **SPECT: normal**

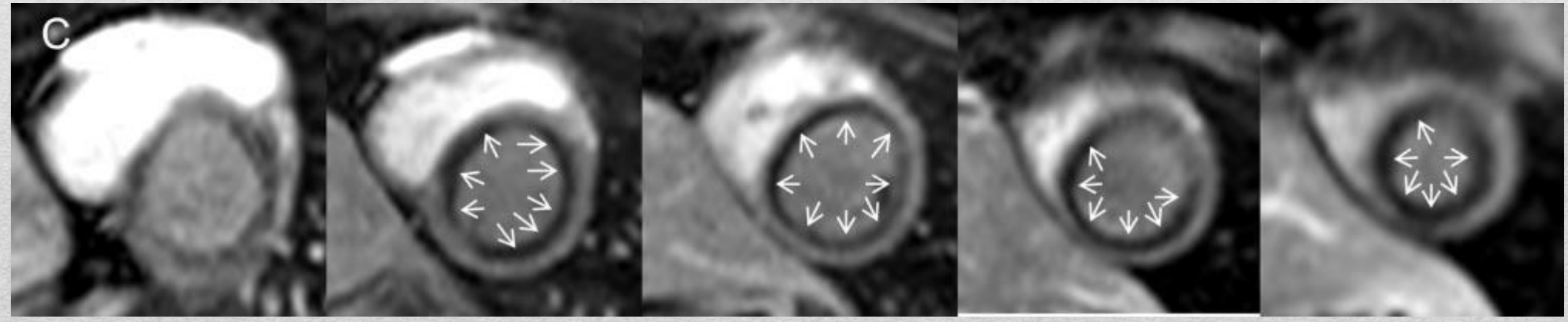
→ Go to stress CMR



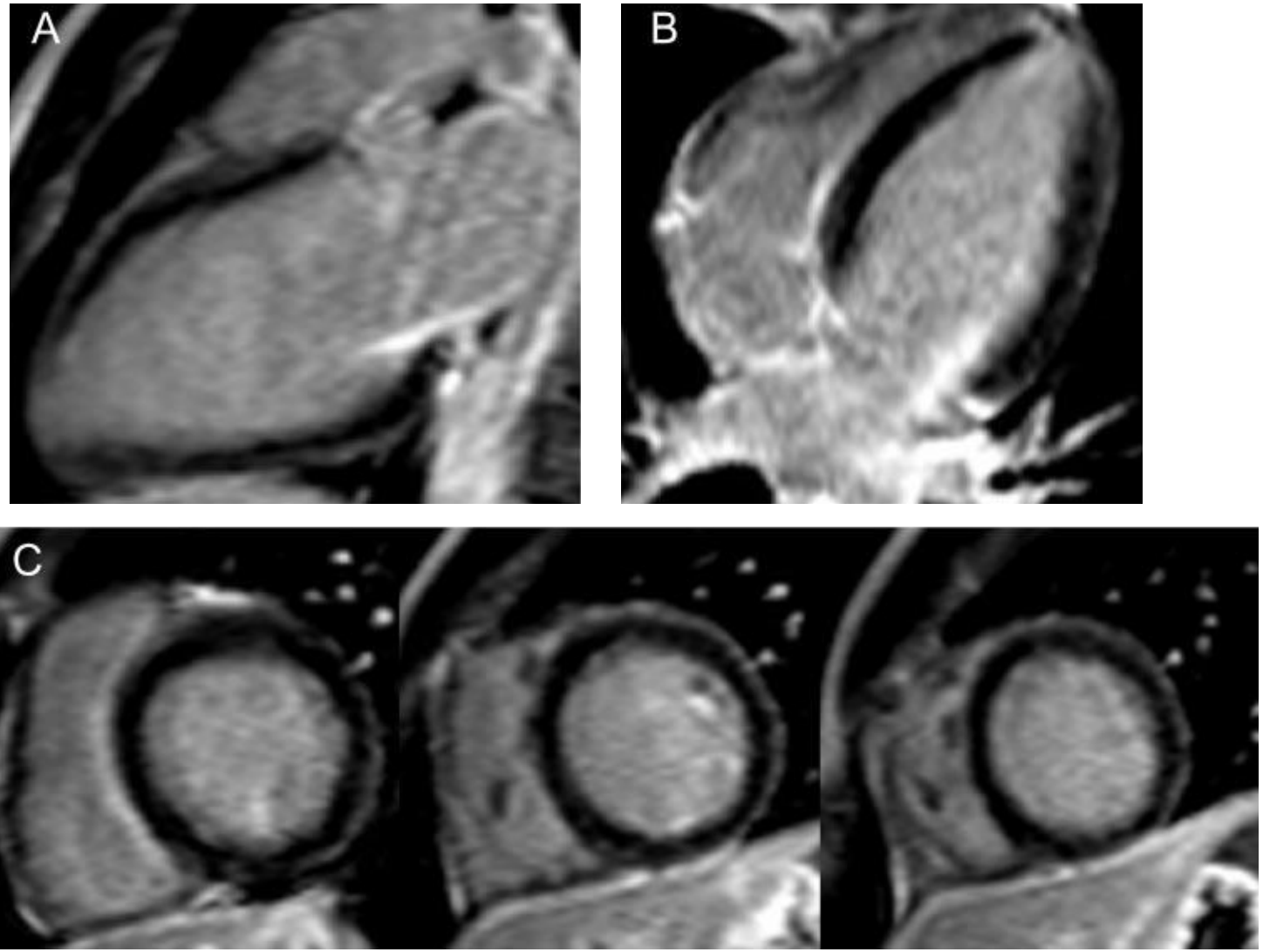
Case report: First pass (inducible ischemia)







Case report: LGE



Coronary angiography revealed high-grade stenoses of the proximal LAD, proximal Cx and RCA.

Inconclusive stress test ??

Circulation: Cardiovascular Imaging

ORIGINAL ARTICLE

Clinical and Economic Implications of Inconclusive Noninvasive Test Results in Stable Patients With Suspected Coronary Artery Disease

Insights From the PROMISE Trial

- **10-25% of all non-invasive stress tests** in clinical routine *(literature)*
- **Worse prognosis** compared to patients with conclusive stress test
- **+140% of medical costs** after 2 years

Prescribe another Stress test !!

Goyal et al. Circulation CV Img. 2020

Management of silent ischemia

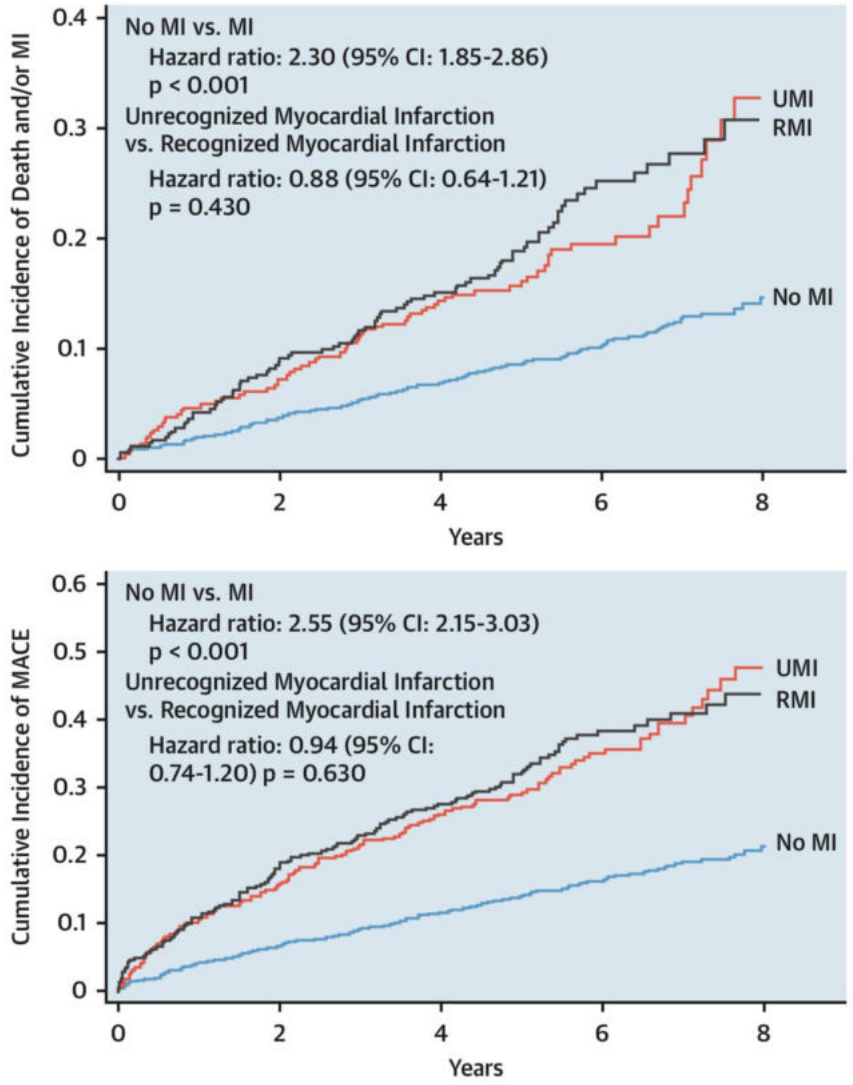
In an asymptomatic patient with CKD and discovery of a silent ischemia?

- **Reinforce the treatment of CV risk factors** in particular dyslipidemia (increased statin dose? add Ezetimibe?) and diabetes mellitus…
- **ACEi +++** (specially if non controlled hypertension, diabetes,…)
- **i-SGLT2 +++** (specially if diabetes, history of heart failure)
- **Consider an anti-ischemic treatment** (beta-blocker?).
- **Consider coronary revascularization,** specially in the case of severe three-vessel CAD or LV dysfunction.

« Unrecognized myocardial infarction » to detect CAD

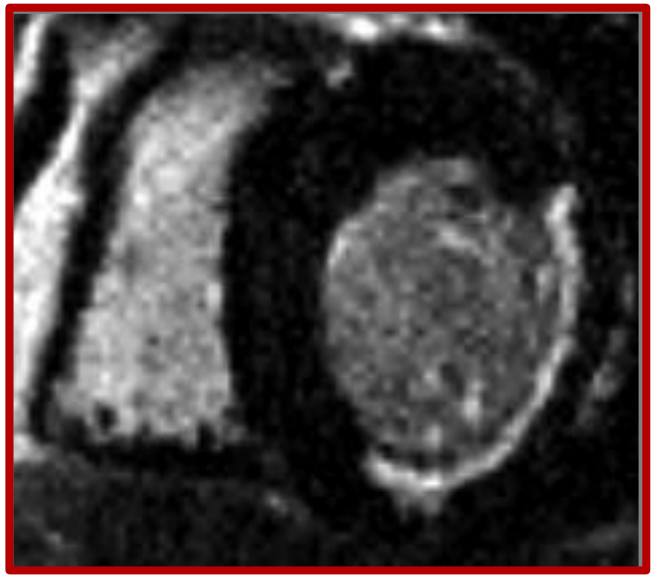
Pronostic value of Unrecognized MI

CENTRAL ILLUSTRATION Time-to-Event Curves for Death and/or MI and MACE



Antiochos, P. et al. J Am Coll Cardiol. 2020;76(8):945-57.

METHODS In the multicenter SPINS (Stress CMR Perfusion Imaging in the United States) study, 2,349 consecutive patients (63 ± 11 years of age, 53% were male) with suspected CAD were assessed by stress CMR and followed over a median of 5.4 years. UMI was defined as the presence of late gadolinium enhancement consistent with MI in the absence of medical history of MI. This study investigated the association of UMI with all-cause mortality and nonfatal MI (death and/or MI), and major adverse cardiac events (MACE).



Antiochos et al. JACC 2020

Coronary artery disease in Symptomatic CKD patients

Safety and Incremental Prognostic Value of Stress CMR in Patients with Known Chronic Kidney Disease

Théo Pezel[1,2,3], Thierry Unterseeh[1], Thomas Hovasse[1], Philippe Garot[1], Solenn Toupin[4], Francesca Sanguineti[1], Stéphane Champagne[1], Tania Ah-Sing[3], MD; Alyssa Faradji[3], Martin Nicol[1,3], Lounis Hamzi[3], Jean Guillaume Dillinger[1], Patrick Henry[1], Valérie Bousson[3] and Jérôme Garot[1].

[1] Cardiovascular Magnetic Resonance Laboratory, ICPS, Massy, France
[2] Department of Cardiology, Lariboisiere Hospital–APHP, Paris, France
[3] Department of Radiology, Lariboisiere Hospital–APHP, Paris, France
[4] Siemens Healthcare France, Saint-Denis, France

Pezel T et al. Journal of Cardiovasc Magnetic Resonance 2023. accepted

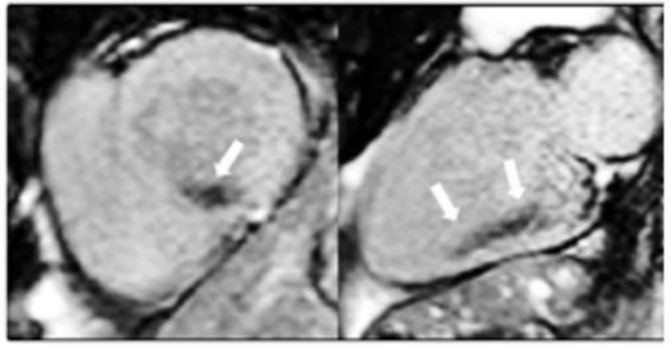
Methods

Study population

- Bi-centre retrospective study from January 2008 to December 2021
- **All consecutive symptomatic** patients **with known CKD** (defined by eGFR <60 ml/min/1.73 m^2) but **without known CAD**, referred for stress CMR.

Stress CMR

- Vasodilator agent: dipyridamole (ICPS) – adenosine (Lariboisiere)
- 1.5T CMR scanner
- First pass perfusion imaging to detect inducible ischemia
- LGE imaging to detect myocardial infarction

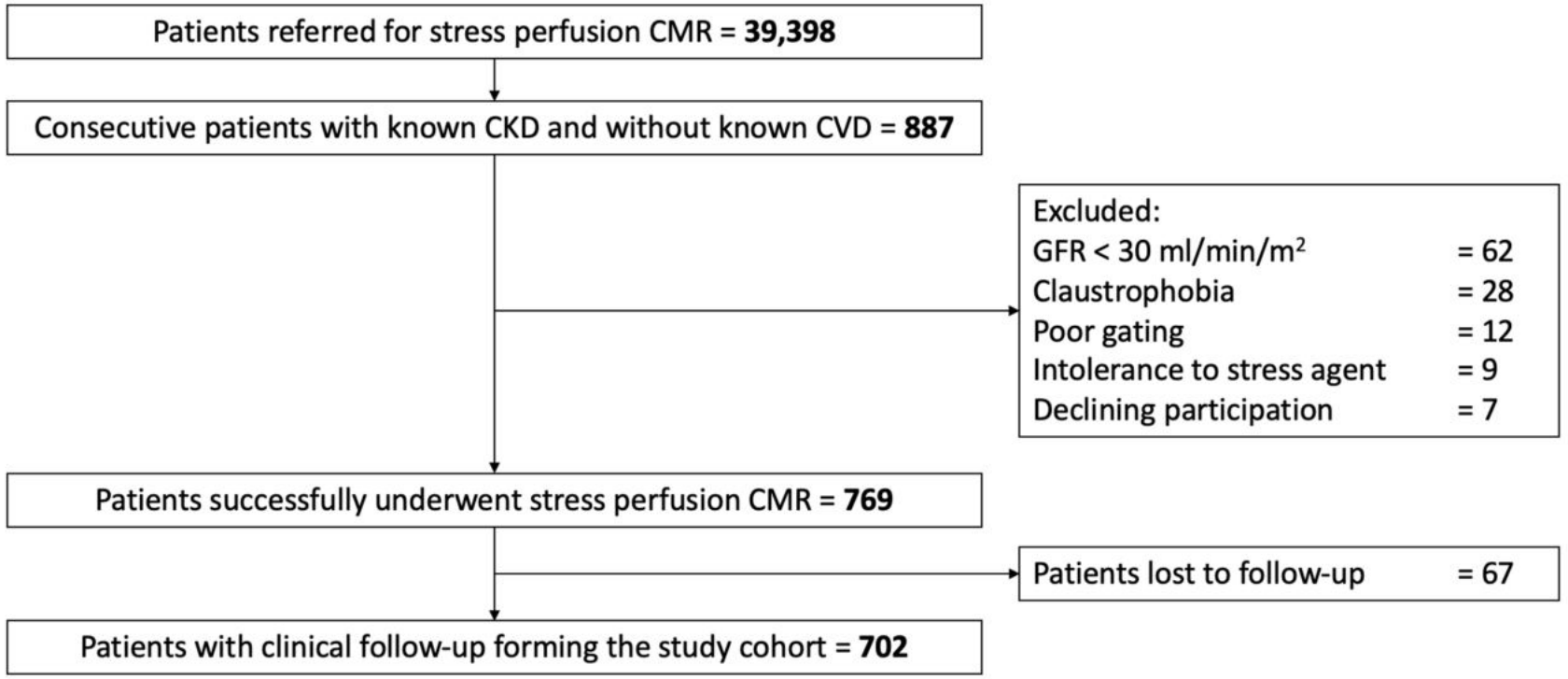


Primary outcome: MACE

- Non-fatal myocardial infarction or CV death

Pezel T et al. Journal of Cardiovasc Magnetic Resonance 2023. accepted

Flow chart



- Stress CMR was **well tolerated** without occurrence of severe adverse event related to the injection of gadolinium.
- **No nephrogenic systemic fibrosis** case.

Pezel T et al. Journal of Cardiovasc Magnetic Resonance 2023. accepted

Baseline characteristics

Table 1. Baseline and CMR characteristics of CKD patients with or without inducible ischemia (N=702)

	All patients (N=702)	Without ischemia (N=557)	With ischemia (N=145)	p value
Demographics				
Age, years	71.4 ± 8.8	71.3 ± 8.8	71.7 ± 8.8	0.64
Male, n (%)	492 (70.1)	392 (70.4)	100 (69.0)	0.46
Body mass index, kg/m²	26.8 ± 3.2	27.0 ± 3.3	26.0 ± 2.6	**<0.001**
Cardiovascular risk factors, n (%)				
Diabetes mellitus	347 (49.4)	255 (45.8)	92 (63.5)	**<0.001**
Hypertension	525 (74.8)	413 (74.1)	112 (77.2)	0.51
Dyslipidemia	411 (58.5)	326 (58.5)	85 (58.6)	1.00
Current or previous smoking	107 (15.2)	86 (15.4)	21 (14.5)	0.88
Family history of CAD	54 (7.7)	51 (9.2)	3 (2.1)	**0.007**
Obesity (BMI ≥30 kg/m²)	84 (12.0)	80 (14.4)	4 (2.8)	**<0.001**
Time between CKD diagnosis and CMR, years	3.6 ± 2.9	3.2 ± 2.8	5.4 ± 3.1	**<0.001**
eGFR, ml/min/1.73 m²	41 ± 9	43 ± 9	36 ± 10	**<0.001**
Ten-year risk for fatal CAD (%)*	3.6 (1.0–5.9)	3.5 (0.9–5.8)	4.2 (1.2–6.3)	**<0.001**
Indications to stress CMR, n (%)				
Symptomatic angina	618 (88.0)	513 (92.1)	105 (72.4)	**<0.001**
Dyspnea	88 (12.0)	44 (7.9)	44 (30.3)	**<0.001**
Stress CMR findings				
LV ejection fraction, %	62.8 ± 9.8	62.8 ± 9.1	62.8 ± 12.1	0.97

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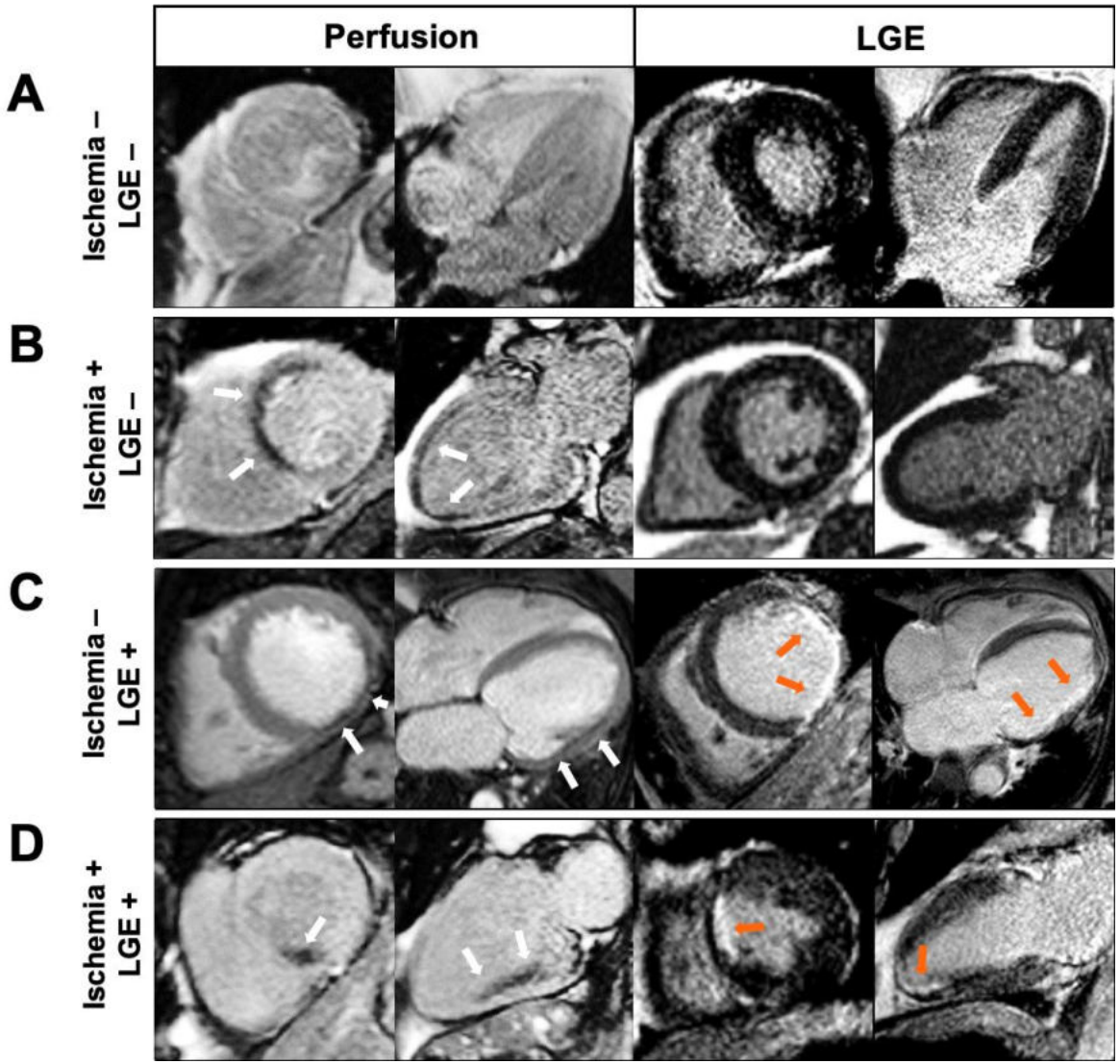
Examples of stress CMR in patients with known CKD



Panel A: normal. 77-year-old male with hypertension and history of CKD (GFR 38 ml/min/m^2), presenting atypical angina.

Panel B: inducible ischemia. 69-year-old female with and history of CKD (GFR 56 ml/min/m^2), presenting dyspnea on exertion.

Panel C: myocardial scar without ischemia. 70-year-old female with diabetes mellitus, hypertension and history of CKD (GFR 41 ml/min/m^2), presenting dyspnea on exertion.

Panel D: myocardial scar with additional inducible ischemia. 67-year-old male with diabetes mellitus, hypertension and history of CKD (GFR 55 ml/min/m^2), presenting atypical angina.

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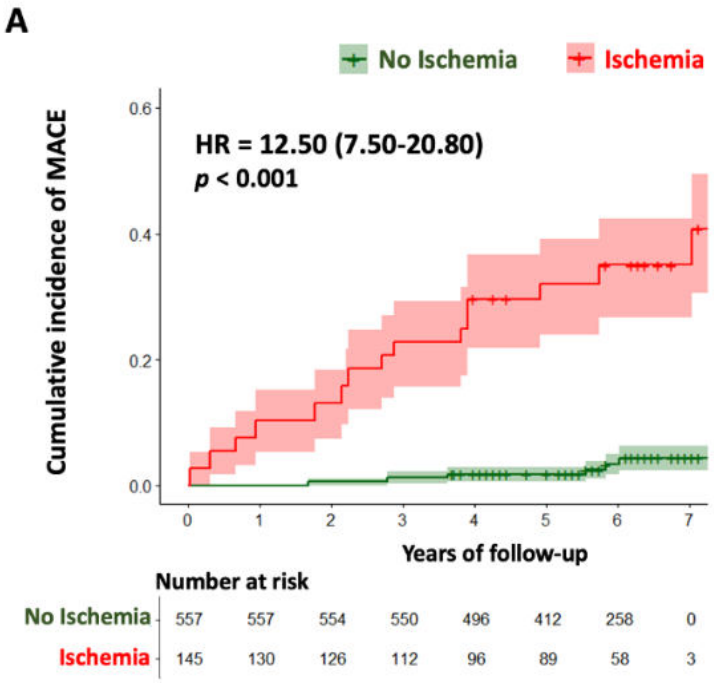
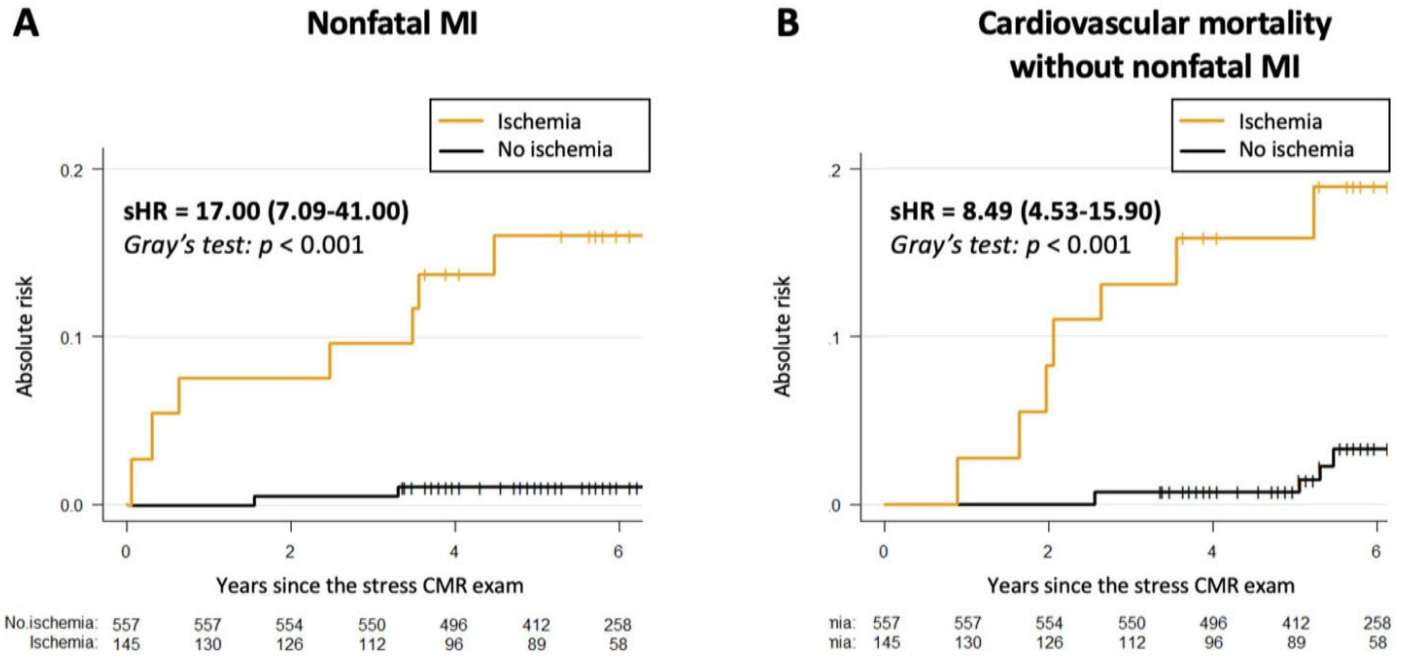
Results

Results: Prognostic value of Inducible ischemia in CKD patients



Traditional Cox model



Competing risk model (Fine and Gray)

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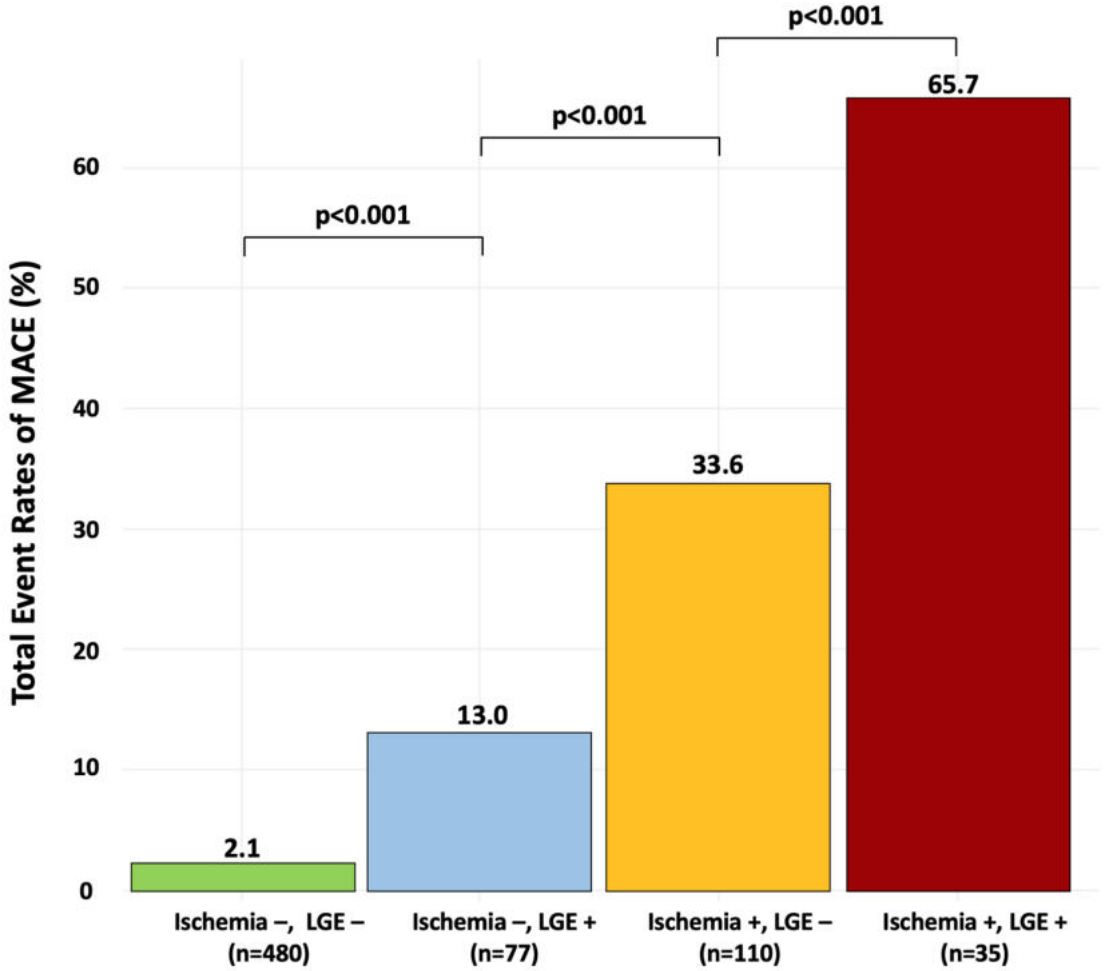
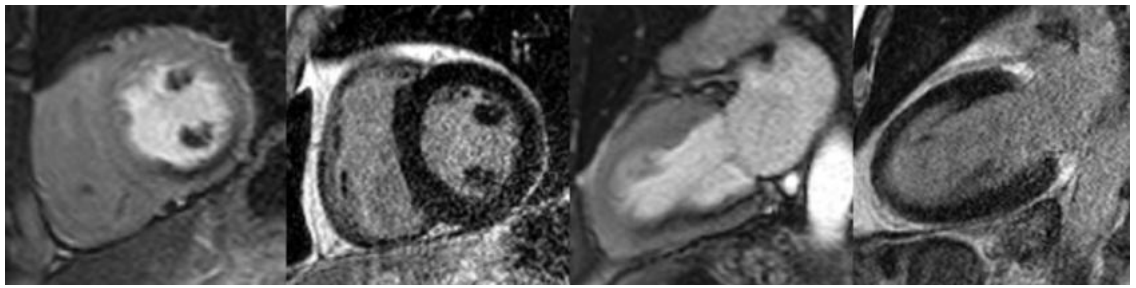
Results

Results: Prognostic value of both Inducible ischemia and LGE in CKD patients





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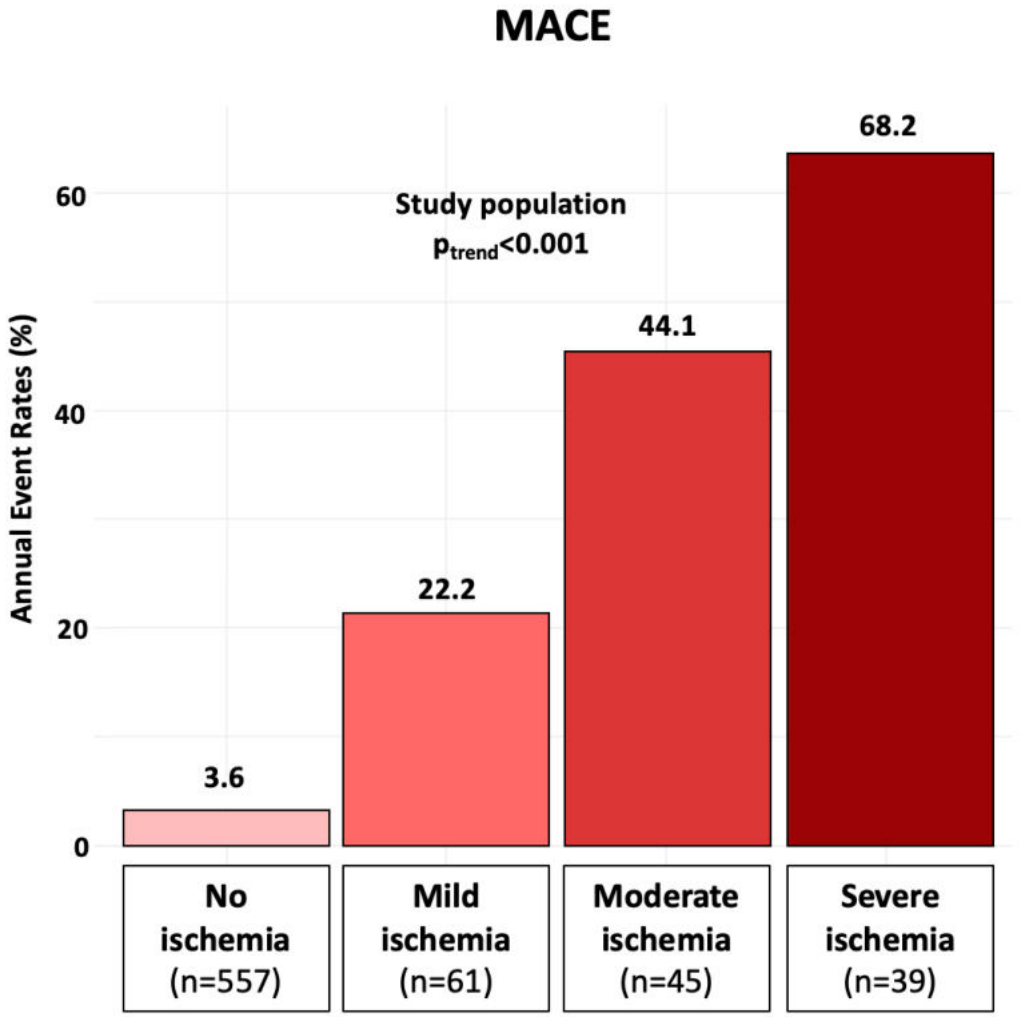
Results

Results: Prognostic value of the extent of Inducible ischemia in CKD patients



Mild, moderate, and severe ischemia were defined as the involvement of 1 to 2, 3 to 5, and ≥6 myocardial segments, respectively.

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Results

Results: Multivariable Cox regression analysis for the prediction of MACE

	MACE		Cardiovascular Mortality	
	Hazard Ratio (95% CI)	**p value**	**Hazard Ratio (95% CI)**	**p value**
Model 1*				
Age	1.02 (0.99-1.06)	0.17	1.09 (1.05-1.15)	**<0.001**
Male	0.86 (0.51-1.48)	0.59	0.80 (0.48-1.46)	0.67
Body mass index	1.05 (0.99-1.13)	0.12	1.04 (0.95-1.14)	0.397
Diabetes mellitus	5.22 (0.88-9.50)	**<0.001**	8.27 (3.59-19.1)	**<0.001**
Hypertension	3.66 (1.99-6.73)	**<0.001**	5.50 (2.26-13.4)	**<0.001**
Dyslipidemia	0.77 (0.51-1.25)	0.63	0.59 (0.30-1.08)	0.09
Current or previous smoking	2.81 (1.55-5.11)	**<0.001**	1.36 (0.62-3.09)	0.28
Family history of CAD	1.08 (0.47-2.46)	0.78	1.90 (0.78-4.50)	0.35
LVEF	0.92 (0.72-1.19)	0.54	0.87 (0.66-1.22)	0.68
eGFR	0.83 (0.61-0.97)	**0.03**	0.71 (0.52-0.89)	**0.02**
Time between CKD diagnosis and CMR exam	1.62 (0.91-2.59)	0.19	1.99 (0.91-4.40)	0.10
Model 2†				
Presence of unrecognized MI	5.07 (3.13-8.21)	**<0.001**	6.15 (2.98-12.1)	**<0.001**
Model 2bis†				
Presence of inducible ischemia	16.4 (8.31-34.2)	**<0.001**	8.22 (3.08-26.2)	**<0.001**
Model 3‡				
Presence of unrecognized MI	4.67 (2.83-7.68)	**<0.001**	6.21 (3.10-12.5)	**<0.001**
Presence of inducible ischemia	15.5 (7.72-30.9)	**<0.001**	7.67 (2.61-22.6)	**<0.001**
Model 4§				
Presence of unrecognized MI	4.60 (2.80-7.66)	**<0.001**	6.02 (2.89-11.8)	**<0.001**
Number of segments of inducible ischemia	1.19 (1.10–1.29)	**<0.001**	1.11 (1.04–1.52)	**0.021**

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Results

Results: Incremental prognostic value of stress CMR findings

	MACE		
	C-index (95%CI)	**NRI (95%CI)**	**IDI (95%CI)**
Model 1 (traditional CV risk factors) *	0.74 (0.69-0.78)	Reference	Reference
Model 2 (model 1 + unrecognized MI) †	0.82 (0.76-0.87)	0.250 (0.067-0.440)	0.035 (0.018-0.060)
Model 3 (model 2 + inducible ischemia) ‡	0.87 (0.83-0.90)	0.477 (0.236-0.678)	0.049 (0.025-0.071)

* **Model 1** included traditional CV risk factors: age, male, BMI, diabetes mellitus, hypertension, dyslipidemia, current or previous smoking, family history of CAD, LVEF, GFR, and time between CKD diagnosis and CMR exam.

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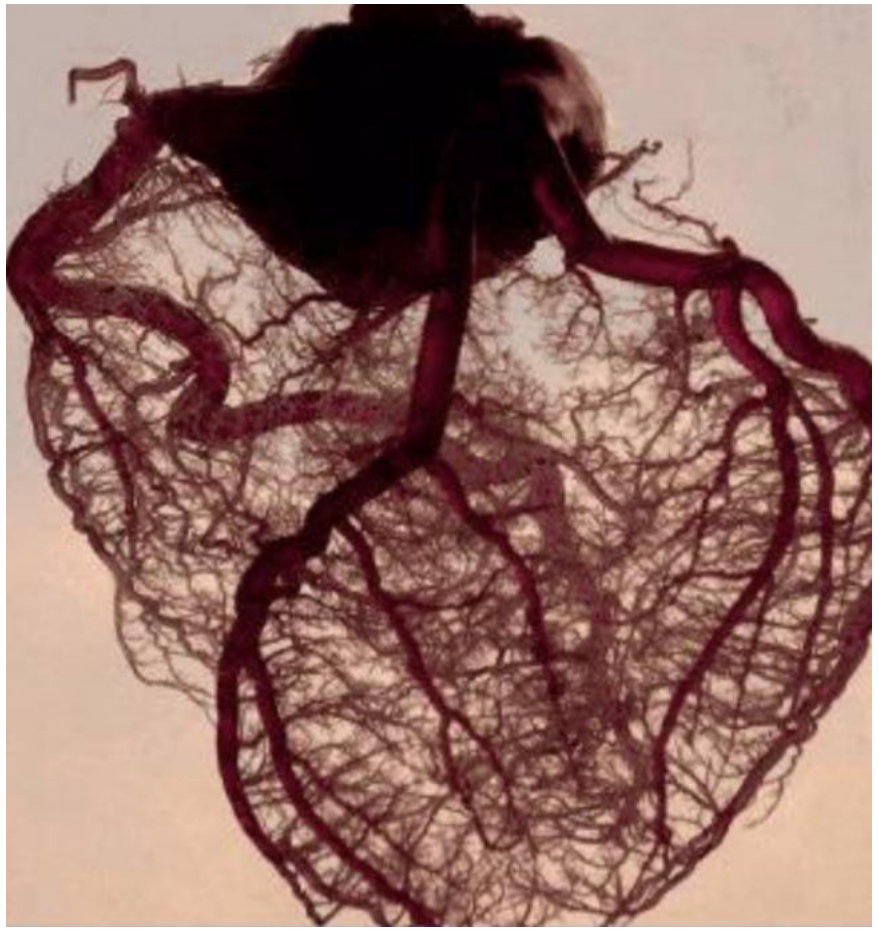
Conclusion

Main findings

- In symptomatic patients with known CKD but without known CAD, stress CMR is **feasible** and **safe**.
- Inducible myocardial ischemia and unrecognized MI by stress CMR were independently associated with CV mortality or nonfatal MI.
- Stress CMR findings had an **incremental prognostic value** above traditional risk factors for predicting the occurrence of MACE.

Pezel T et al. Journal of Cardiovasc Magnetic Resonance 2023. accepted

Microvascular angina



ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1–71
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2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

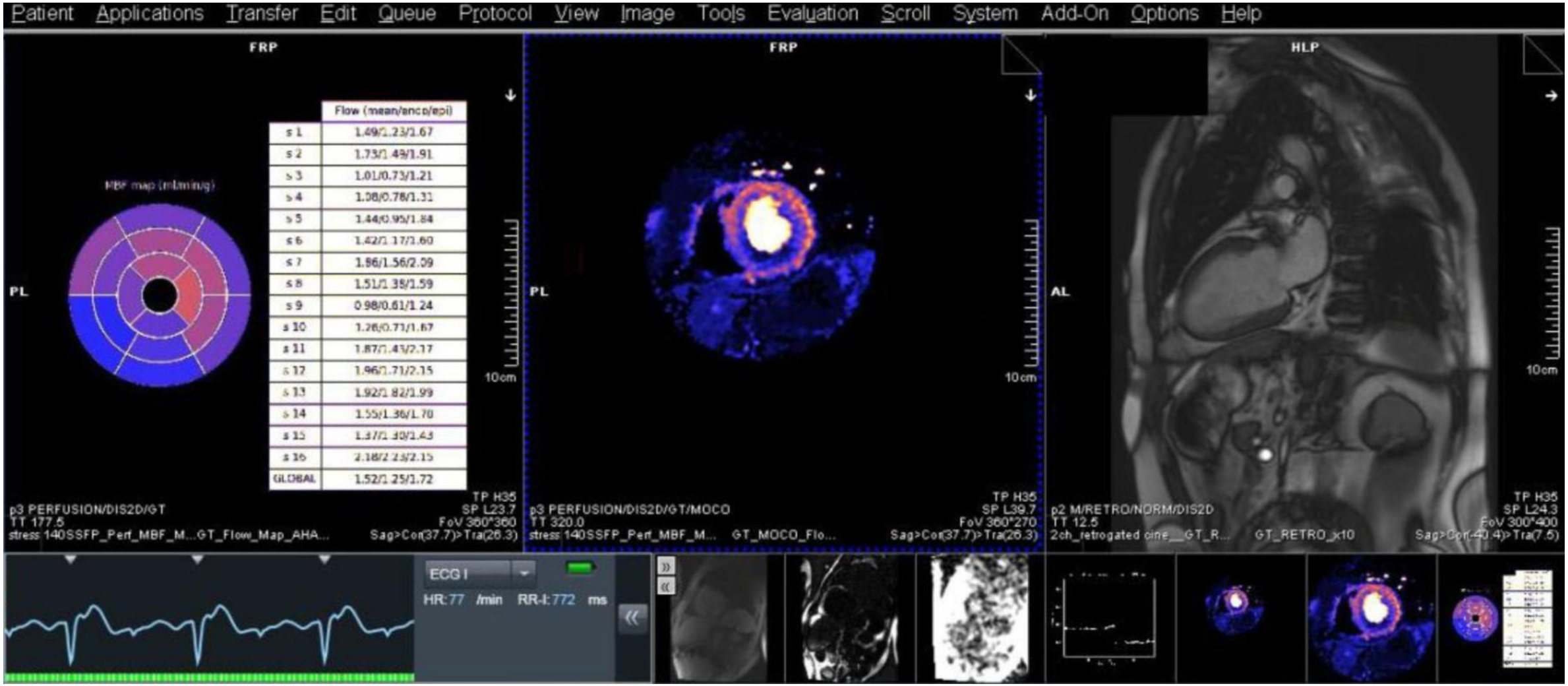
6.1 Microvascular angina

Patients with microvascular angina typically have exercise-related angina, evidence of ischaemia in non-invasive tests, and either no stenoses or mild-to-moderate stenoses (40–60%), revealed by ICA or CTA, that are deemed functionally non-relevant.[415] Given the similarity of angina symptoms, a microvascular origin of angina is typically suspected, after excluding obstructive epicardial coronary stenoses, during diagnostic workup of patients with suspected myocardial ischaemia. Regional LV wall motion abnormalities rarely develop during exercise or stress in patients with microvascular angina.[412,416] Some patients may also have a mixed pattern of angina, with occasional episodes at rest, particularly associated with exposure to cold.

Investigations in patients with suspected coronary microvascular angina

Recommendations	Class[a]	Level[b]
Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR.[412,413]	IIa	B
Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.[412,438–440]	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.[430–432,441]	IIb	B

Cardiac MRI with Quantitative Perfusion



Courtesy Pr. Peter Kellman and Siemens Healthineers

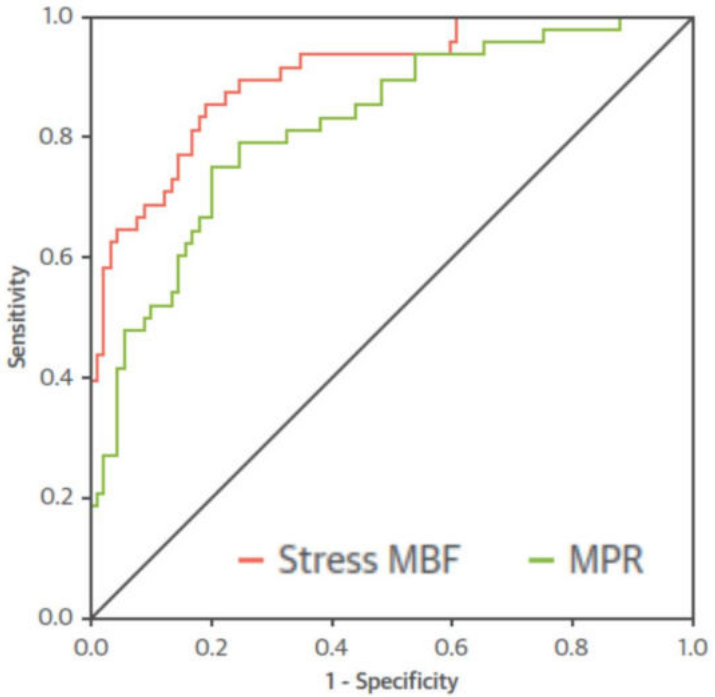
Cardiac MRI with Quantitative Perfusion

ORIGINAL RESEARCH

Automated Pixel-Wise Quantitative Myocardial Perfusion Mapping by CMR to Detect Obstructive Coronary Artery Disease and Coronary Microvascular Dysfunction

Validation Against Invasive Coronary Physiology

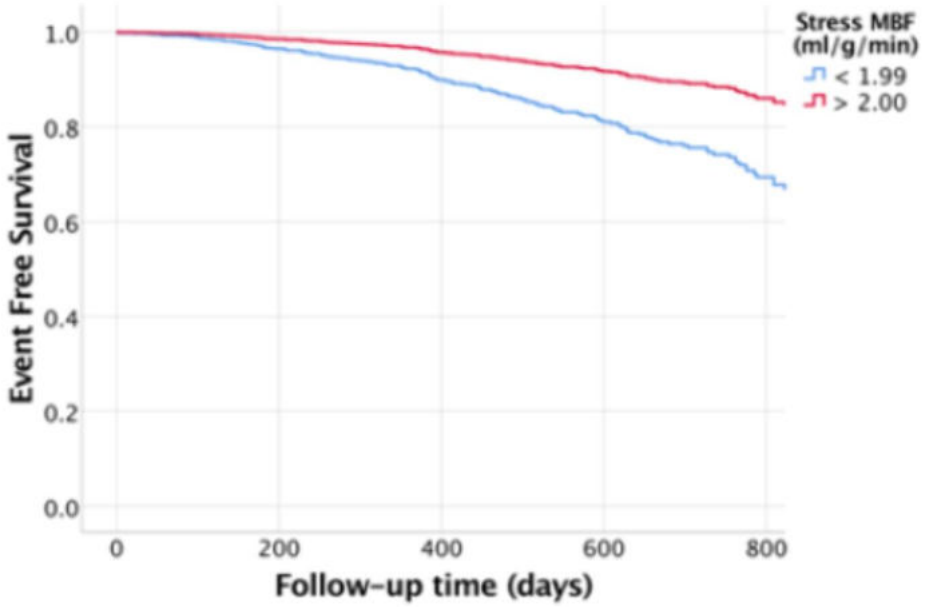
Tushar Kotecha, MBChB,[a,b,*] Ana Martinez-Naharro, MD,[b,c,*] Michele Boldrini, MD,[c] Daniel Knight, MD,[a,b] Philip Hawkins, PhD,[b,c] Sundeep Kalra, PhD,[b] Deven Patel, MD,[b] Gerry Coghlan, MD,[b] James Moon, MD,[a,d] Sven Plein, PhD,[e] Tim Lockie, PhD,[b] Roby Rakhit, MD,[a,b] Niket Patel, MD,[a,b] Hui Xue, PhD,[f] Peter Kellman, PhD,[f] Marianna Fontana, PhD[b,c]



Circulation

The Prognostic Significance of Quantitative Myocardial Perfusion: An Artificial Intelligence Based Approach Using Perfusion Mapping

Kristopher D. Knott, Andreas Seraphim, Joao B. Augusto, Hui Xue, Liza Chacko, Nay Aung, Steffen E. Petersen, Jackie A. Cooper, Charlotte Manisty, Anish N. Bhuva, Tushar Kotecha, Christos V. Bourantas, Rhodri H. Davies, Louise A.E. Brown, Sven Plein, Marianna Fontana, Peter Kellman, and James C. Moon ✉Institute of Cardiovascular Science, University College London, London, UK; Barts Heart Centre, St Bartholomew's Hospital, London, UKNational Heart, Lung, and Blood Institute, National Institutes of Health, DHHS, Bethesda, MDInstitute of Cardiovascular Science, University College London, London, UK; Royal Free Hospital, London, UKBarts Heart Centre, St Bartholomew's Hospital, London, UK; William Harvey Research Institute, Queen Mary University of London, UKWilliam Harvey Research Institute, Queen Mary University of London, UKDepartment of Biomedical Imaging Science, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Clarendon Way, Leeds, UKInstitute of Cardiovascular Science, University College London, London, UK; 2Barts Heart Centre, St Bartholomew's Hospital, London, UK; Royal Free Hospital, London, UK



Merci pour votre attention

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